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National Conference on

'Emerging Trends in Chemical Science'

(ETCS-2018)

9th & 10th February, 2018

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(ETCS-2018)

9th & 10th February 2018

Venue

Conference Hall, Poona College ,
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The Poona College of Arts, Science & Commerce was established in the year 1970 by Yateemkhana and Madrasa 'Anjuman Khairul Islam', Mumbai, a Philanthropic Charitable Trust dedicated to the noble cause of the orphans and the deprived. Situated prominently in the heart of Pune Camp, it has brought about a revolutionary change in the region's educational scenario, diversified in leaps and bounds and has carved a niche for itself as a celebrated seat of learning. This was humbly acknowledged by the National Assessment and Accreditation Council (NAAC) Bangaluru in the year 2004 which awarded it with the Prestigious 'A' grade and got reaccredited in September 2015.

The College is a recognized Research Centre of the Savitribai Phule Pune University in Chemistry, Commerce, Economics and with full-fledged degree courses and Postgraduate Centers in Organic Chemistry,Computer Science, Electronics, Zoology, Economics, English, Urdu and Commerce. Apart from this, it also offers professional courses of B.B.A, B.C.A, B.Sc. and M.Sc. (Computer Science). Gradually it has expanded on a national as well as global scale with student enrollment exceeding 6000 every year and has become a favoured destination for education seekers from all Indian states particularly the North-East and from over 15 countries abroad.

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There is a prodigious development of every field of science in recent decades because of rapid progress and advancement in different areas of chemical sciences. The primary goal of the conference is to promote research and developmental efforts undertaken in the arena of chemical sciences. The scheduled conference organized at Y & M AKI’s Poona College of Arts, Science & Commerce, Pune will definitely offer a scientific platform to exchange and explore the latest information on the emerging trends in the field of chemical science and help to connect the teaching and scientific communities together for the fruitful development in various fields of research. The conference will provide opportunities for scientists, researchers and students to exchange the first hand information and experience in thrust area of current research.

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INDEX

Synthesis And Characterization Of Isomeric Triplet Drug Type Molecules Containing Pyridine And Thiazole Nucleus

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Abstract: *A library of isomeric pyridyl - thiazoles were synthesized by employing consecutive Hantzsch Thiazole synthesis. Amongst the three isomeric series, 2-pyridyl and 4-pyridyl isomers were found to exhibit better drug like properties than 3-pyridyl series. Pharmacokinetic properties of these derivatives have been studied using Lipinski's Rule of five (RO5) to predict the bioactivity score. Almost all compounds followed the criteria for orally active drug and hence showed good drug like properties.*

Keywords: *Hantzsch thiazole synthesis, photo physical properties, Lipinski's rule of five .*

1. INTRODUCTION:

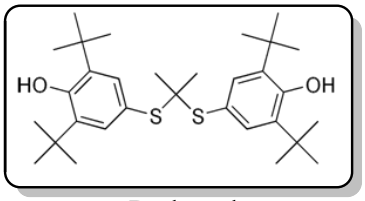
1,3-Azoles (imidazole, oxazole and thiazole) are very stable compounds which do not auto-oxidise. Thiazole is an asymmetrical molecule compared with thiophene and the two alpha positions of sulphur atom have distinguishable reaction activities. Synthesis of this asymmetric thiazole containing compounds remains more challenging than the symmetrical thiazole molecule. Thiazole ring is highly reactive due to the presence of an acidic proton at C-2 and has emerged as an important synthon to generate variety of NCEs (New Chemical Entities). Diverse modification of the thiazole ring at various positions led to a variety of novel compounds with wide spectrum of pharmacological activities. Thiazole and its derivatives have attracted continuing interest to design novel CNS active agents. Thiazole occupy a prominent position possessing a broad range of biological activities , found in a wide variety of bioactive molecules and natural products[1] such as vitamin thiamine, Sulfathiazol (antimicrobial drug), Ritonavir (antiretroviral drug), Abafungin (antifungal drug) and Triazofurine (antineoplastic drug). Thiazole and its derivatives possess almost all biological and pharmacological activities like antibacterial, antiprotozoal, antimalarial, anticancer[2],treat allergies[3], gene-modulating activities, antischizophrenia, antihypertension [4], anti-inflammation [5], anti-HIV infections [6] and many more.

Pyridine is an important six membered heterocycle which has found many applications in medicinal chemistry. They are at the center in the biological activity of natural substances including vitamine B_6, nicotine or oxido-reductive NADP-NADPH coenzymes. Pyridine containing complex natural products also exist in the sesquiterpene, alkaloid, enediyne or polypeptide families. Other bioactive pyridines have been syntheised resulting in efffects like antiinflammatory [7], antiasthamatic [8], antidepressant [9], acetylcholnesterase inhibitory [10], treating hypertension [11] or hypotension [12], inhibiting HIV protease [13], preventing [14] or inducing apoptosis [15]. Thus this nucleus is an important constitute for the formation of antitumor or antiviral drugs. Not only pharmaceutical but also in agro-chemistry [16] pyridine plays an important role for their herbicide [17], insecticide [18] and antifungal [19] properties.

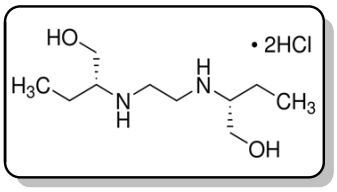
The term therapeutic index indicates how safe a particular drug is. It is a measure of the drugs beneficial effects at a low dose versus its harmful effects at a high dose. A high therapeutic index means that there is a large safety margin between beneficial and toxic doses. Single drug is used for the treatment of particular disease at particular dose level. Sometimes at that particular dose level, it shows some side effects. So in order to minimise the side effects , one has to decrease the dose of that drug and give another drug in combination with that drug having the similar effect. Mostly the side effects are dose dependent, so if dosage is decreased the side effects are automatically reduced. In marketed tablets two powders of different drugs are combined. During this combination the lipophilicity of the drugs do not increased but when they are given in the form of derivative, lipophilicity is increased and bioavilability is enhanced. The dosing of both the drugs will decrease because of the synergistic effect.

Twin and triplet drugs are defined as compounds that contain respectively two and three pharmacophore components exerting pharmacological effects in a molecule. The twin drug bearing the same pharmacophores is a "symmetrical twin drug", whereas that possessing different pharmacophores is a "non-symmetrical twin drug." In general, the symmetrical twin drug is expected to produce more potent and / or selective pharmacological effects, whereas the non-symmetrical twin drug is anticipated to show both pharmacological activities stemming from the individual pharmacophores (dual action). On the other hand, non-symmetrical triplet drugs, which have two of the same pharmacophores and one different moiety, are expected to elicit both increased pharmacological action and dual action. The two identical portions could bind the same receptor sites simultaneously while the third portion could bind a different receptor site or enzyme.

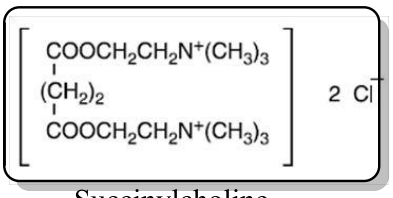
Symmetrical twin drugs :



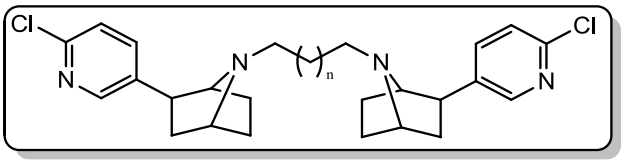
Probucol
Antihyperlipoproteinemic



Ethambutol
Tuberculostic



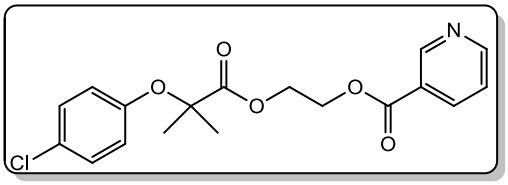
Succinylcholine
Skeletal muscle relaxant



Epibatidine
Acetylcholine inhibitor
Linker mode

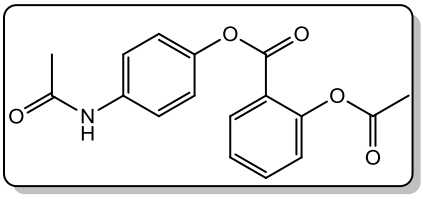
Nonsymmetrical twin drugs :

Clofibric acid + Nicotinic acid →



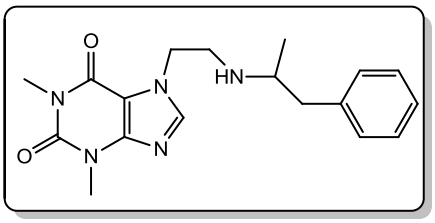
Etofibrate (Linker mode)

Paracetamol + Aspirin →



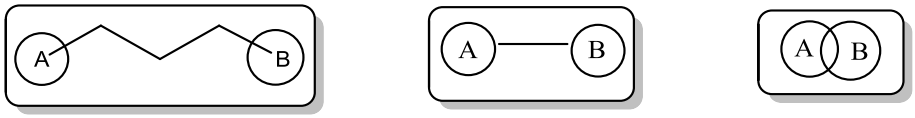
Benorylate (No linker mode)

Cafeine + Amphetamine →



Etofibrate (Linker mode)

Twin drugs which are hybrids and are found in many natural products with potent bioactivity. Combining two active compounds in a single molecule increases interactions with biological targets and provide desired multiple or complementary mode of action. Such compounds are new chemical entities with their individual and own pharmacokinetic and pharmacodynamic properties. The combination of two identical or non-identical pharmacophore can also be classified by the type of connection : "Linker mode" ,"No linker mode" and "overlap mode"



A and B may be identical or nonidentical pharmacophore

Compounds containing two thiazole rings also reported to possess various biological activity such as anti-inflammatory, anti-bacterial, anti-viral. The search for new biologically active di-thiazole analogues continues to be an area of intensive investigation in medicinal chemistry. Di-thiazole nucleus has been established as the potential entity in the largely growing chemical world of heterocyclic compounds possessing promising pharmacological characteristics. Di-thiazole compounds and their various derivatives play a vital role in nature. For example, the thiazolium ring present in the vitamin B1 serves as an electron sink and its co-enzyme form is important for the decarboxylation of keto acids. This heterocyclic system has found broad applications in drug development for the treatment of allergies, inflammation, hypertension, bacterial and HIV infections. Dithiazole derivatives have been shown to possess anticancer activity [19] and potential Hepatitis C Virus NS5A inhibitor activity [20] in replicon systems.

With the above consideration of non-symmetrical twin drugs (no linker mode) and importance of polyaromatic hydrocarbons, in this study we report the synthesis of isomeric penta-aromatic compounds containing pyridine and two thiazole rings. This range of analogues **(a-x)** are subjected to study for Lipinski parameters.

2. MATERIALS AND METHOD :

2.1. General Remarks

Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorected. All the reactions were monitored by thin layer chromatography (TLC) on precoated silica gel 60 F254(mesh); spots were visualized with UV light. Merck silica gel(60-120 mesh) was used for column chromatography. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Brucker Avance II 400 MHz NMR spectrometer in $CDCl_3$/DMSO-d_6 solution using tetramethylsilane as an internal standard. All chemical shifts were recorded in δ (ppm) and the following abbreviations are used: s, singlet; d, doublet; dd, doublet of doublet; t, triplet; m, multiplet.

2.2.General procedure for the synthesis of isomeric pyridine-thioamides (2)

A solution of pyridine carbonitriles (**1**) (5gm/5ml, 48 mmol) in pyridine (15 ml) and triethyl amine (3 ml) was stirred for 15 min. H_2S gas was then passed into the reaction mixture for 2 hr. As the reaction proceed, the colour of the solution initially turns green and then turns into greenish yellow solid. The reaction was monitored on TLC. After completion of the reaction, the mixture was poured onto crushed ice. The crude thioamide product (**2**) was filtered and washed extensively with water. The product was re-crystallized from ethanol to obtain almost pure product. Colour – greenish yellow, Yield: 4-5gm, 80-90%.

2.3.General procedure for the synthesis of isomeric-pyridyl- thiazol- benzonitriles (3)

To a solution of thioamides (**2**) (5g, 36mmol) in ethyl alcohol (20 ml), 4-cyano phenacyl bromide (8gm, 36mmol) was added and the reaction was refluxed on the hot plate. After the completion of the reaction as monitored on TLC (3 hr), the reaction mixture was poured in cold water. The solid crude product (**3**) obtained was filtered, washed with water and dried. The product obtained was sufficiently pure and was used as such for the next stage, Yield: 9.75, 75.39%.

2.4.General procedure for the synthesis of isomeric-pyridyl- thiazol- benzothioamides (4)

Compound (**3**) (5gm, 25 mmol) was dissolved into pyridine (15ml) and triethyl amine (3ml). The reaction was then stirred for 15 min. H_2S gas was then passed into the reaction mixture for 3hr. The reaction was monitored on TLC. The solid greenish yellow product obtained was filtered and washed with water. The product was used without purification for the next stage. Colour – greenish yellow, Yield: 4.70, 94%.

2.5.General procedure for the synthesis of pentameric isomers of pyridine (5) (a-x)

To a solution of compound (**4**) (0.5gm, 2.5 mmol) in ethyl alcohol, 4-substituted phenacyl bromide (2.5mmol) was added and the reaction was refluxed on the hot plate. After completion of the reaction as monitored on TLC (3 hr), the solvent was evaporated and the reaction mixture was poured onto crushed ice. The crude product (**a-x**) thus obtained was filtered, washed with water and dried. The crude product was re-crystallized from ethanol and purified by column chromatography technique using hexane and ethyl acetate.

4-phenyl-2-(4-(2-(pyridin-2-yl)thiazol-4-yl)phenyl)thiazole (a)

Yield 77% , Yellow , M.P. 186 ^{0}C. ^{1}H NMR (400MHz, $CDCl_3$): δ 8.64 (dd, *J* = 4.95 Hz, *J* = 1.82 Hz, 1H, pyridine), 8.31 (ddd, *J* = 4.95 , *J* = 7.76 Hz, *J* = 1.21, 1H, pyridine), 8.26 (s, 1H, thiazole), 8.10-8.25 (m , 4H, phenyl),8.06 (d, 1H, thiazole), 8.06 (d, *J* = 7.95 Hz, 2H, Phenyl), 7.98 (dt, *J* = 1.32 Hz, *J* = 7.76 Hz, 1H, pyridine), 7.48 (m, 3H, Phenyl), 7.36 (dd, *J* = 7.76 Hz, *J* = 1.21, 1H, pyridine).

^{13}C NMR (100 MHz, $CDCl_3$) : δ 168.49, 166.45, 155.40, 154.74, 150.44, 149.45, 137.38, 135.55, 133.97,132.61, 128.56, 128.0, 126.11, 124.95, 119.29, 117.68, 114.14.

4-(4-fluorophenyl)-2-(4-(2-(pyridin-2-yl)thiazol-4-yl)phenyl)thiazole (b)

Yield 60% , Yellow , M.P. 196 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 8.94(dd, *J* = 7.57Hz, *J* = 1.78, 1H, pyridine), 8.76 (s, 1H, thiazole), 8.74 (d, *J* = 8.15 Hz, 2H, Phenyl), 8.10-8.30 (m , 4H, phenyl) , 8.14 (d, 1H, thiazole), 8.03 (dd, *J* = 5.57 Hz, *J* = 1.82 Hz, 1H, pyridine), 7.99 (ddd, *J* = 5.57 , *J* = 7.67 Hz,1H, pyridine), 7.54 (dt, *J* = 1.32 Hz, *J* = 7.67 Hz, 1H, pyridine) , 7.48 (d, 2H, *J* = 8.15 Hz, 2H, Phenyl), 7.12 (dd, *J* = 7.67 Hz, *J* = 1.78, 1H, pyridine).

^{13}C NMR (100 MHz, $CDCl_3$) : δ 164.49, 161.45, 158.45, 152.74, 149.41, 147.45, 141.38, 136.55, 133.97,132.61, 129.56, 127.20, 125.11, 121.95, 118.29, 114.68, 112.14.

4-(4-chlorophenyl)-2-(4-(2-(pyridin-2-yl)thiazol-4-yl)phenyl)thiazole (c)

Yield 42% , Yellow , M.P. 194 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 8.84 (dd, *J* = 4.45 Hz, *J* = 1.02 Hz, 1H, pyridine), 8.78 (d, 2H, *J* = 8.06 Hz, Phenyl), 8.34 (d, 1H, thiazole, 8.12 (ddd, *J* = 4.45 , *J* = 7.12 Hz, *J* = 1.21, 1H, pyridine), 8.10-8.40 (m , 4H, phenyl)),8.06 (s, 1H, thiazole), , 8.01 (dt, *J* = 1.02 Hz, *J* = 7.12 Hz, 1H, pyridine), 7.54 (dd, *J* = 7.12 Hz, *J* = 1.21, 1H, pyridine), 7.01 (d, *J* = 8.06 Hz, 2H Phenyl).
^{13}C NMR (100 MHz, $CDCl_3$) : δ 168.49, 164.45, 159.41, 156.75, 149.41, 147.45, 142.38, 138.55, 136.97,131.61, 128.56, 126.0, 124.11, 122.95, 115.29, 113.68, 114.14.

4-(4-bromophenyl)-2-(4-(2-(pyridin-2-yl)thiazol-4-yl)phenyl)thiazole (d)
Yield 68% , Yellow , M.P. 198-200 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 8.54(d, 1H, thiazole), 8.43 (dd, *J* = 5.42 Hz, *J* = 1.61 Hz, 1H, pyridine), 8.27 (s, 1H, thiazole), 8.14 (d, 2H, *J* = 7.76 Hz, Phenyl), 8.12 (ddd, *J* = 5.42, *J* = 8.05 Hz, *J* = 1.61, 1H, pyridine), 8.10-8.20 (m , 4H, phenyl), 7.84 (d, 2H, *J* = 8.06 Hz, Phenyl),7.24 (dt, *J* = 1.57 Hz, *J* = 8.05 Hz, 1H, pyridine), 7.01(dd, *J* = 7.98 Hz, *J* = 1.75, 1H, pyridine).
^{13}C NMR (100 MHz, $CDCl_3$) : δ 167.49, 164.45, 157.4, 154.7, 159.4, 147.45, 144.38, 142.55, 139.97,134.61, 127.56, 125.0, 124.11, 122.95, 120.29, 117.68, 114.14.

2-(pyridin-2-yl)-4-(4-(4-(p-tolyl)thiazol-2-yl)phenyl)thiazole (e)
Yield 90% , White , M.P. 218 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 8.60 (dd, *J* = 5.04 Hz, *J* = 1.82 Hz, 1H, pyridine), 8.39 (ddd, *J* = 5.98, *J* = 7.98 Hz, *J* = 1.75 1H, pyridine), 8.25 (s, 1H, thiazole), 8.10-8.25 (m , 4H, phenyl), 7.98 (d, 1H, thiazole), 7.97 (d, *J* = 8.6 Hz, 2H, Phenyl), 7.98 (dt, *J* = 1.8 Hz, *J* = 7.9 Hz, 1H, pyridine),7.93 (d, *J* = 8.66 Hz, 2H, Phenyl), 7.26 (d, *J* = 7.98 Hz 1H, pyridine).
^{13}C NMR (100 MHz, $CDCl_3$) : δ 168.20, 166.10, 156.0, 155.0, 148.9, 137.8, 136.0, 132.2, 132.30, 128.0, 127.5, 126.23, 124.52, 123.11, 125.71, 119.20, 117.68, 114.05, 22.56.

4-(4-methoxyphenyl)-2-(4-(2-(pyridin-2-yl)thiazol-4-yl)phenyl)thiazole (f)
Yield 76% , White , M.P. 208 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 8.60 (s, 1H, thiazole), 8.46 (s, 1H, thiazole), 8.41 (ddd, *J* = 5.55 , *J* = 1.20 Hz, *J* = 6.77 1H, pyridine), 8.15 (dd, *J* = 5.55 Hz, *J* = 1.20 Hz, 1H, pyridine), 8.10-8.30 (m , 4H, phenyl), 8.06 (d, *J* = 8.45 Hz, 2H, Phenyl), 7.78 (dt, *J* = 1.20 Hz, *J* = 6.77 Hz, 1H, pyridine), 7.48 (d, *J* = 8.45 Hz 2H, Phenyl), 7.36 (dd, *J* = 6.77 Hz, *J* = 1.20, 1H, pyridine).
^{13}C NMR (100 MHz, $CDCl_3$) : δ 170.84, 162.95 ,154.23, 153.56, 152.36, 148.95, 147.35, 143.32, 134.45, 133.32, 133.21, 130.62, 128.96, 128.54, 128.41, 124.32,116.32,115.21, 110.21, 55.85.

4-(4-nitrophenyl)-2-(4-(2-(pyridin-2-yl)thiazol-4-yl)phenyl)thiazole (g)
Yield 79% , Yellow , M.P. 200-204 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 8.41 (dd, *J* = 6.51 Hz, *J* = 1.89 Hz, 1H, pyridine), 8.38 (ddd, *J* = 6.51 , *J* = 6.98 Hz, *J* = 1.89 1H, pyridine), 8.26 (s, 1H, thiazole), 8.10-8.25 (m , 4H, phenyl),8.06 (d, 1H, thiazole), 8.06 (d, *J* = 8.03, 2H, Phenyl), 7.98 (dt, *J* = 1.89 Hz, *J* = 6.98 Hz, 1H, pyridine), 7.48 (d, *J* = 8.03, 2H, Phenyl), 7.36 (dd, *J* = 6.98 Hz, *J* = 1.89, 1H, pyridine).
^{13}C NMR ($CDCl_3$) : δ 167.49, 164.45, 157.4, 154.7, 149.4, 147.45, 139.38, 134.55, 131.97,129.61, 128.56, 124.0, 122.11, 119.95, 117.29, 114.68, 111.14.

4-(2-(4-(2-(pyridin-2-yl)thiazol-4-yl)phenyl)thiazol-4-yl)benzonitrile (h)
Yield 97% , White , M.P. 242 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 8.94 (dd, *J* = 4.95 Hz, *J* = 1.82 Hz, 1H, pyridine), 8.56 (ddd, *J* = 4.95 , *J* = 7.76 Hz, *J* = 1.21 1H, pyridine), 8.45 (s, 1H, thiazole), 8.30-8.41 (m , 4H, phenyl), 8.32 (d, 1H, thiazole), 8.02 (m, 2H, Phenyl), 7.88 (dt, *J* = 1.32 Hz, *J* = 7.76 Hz, 1H, pyridine), 7.35 (m, 3H, Phenyl), 7.26 (dd, *J* = 7.76 Hz, *J* = 1.21, 1H, pyridine).
^{13}C NMR ($CDCl_3$) : δ 162.53, 159.05, 143.14, 153.7, 149.4, 146.45, 133.38, 135.05, 123.37,141.33, 128.41, 131.0, 127.51, 123.43, 145.91, 112.68, 115.14.

4-phenyl-2-(4-(2-pyridin-3-yl)thiazol-4-yl)phenyl)thiazole (i)
Yield 56% , Yellow , M.P. 178 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 9.12 (m, 1H, pyridine), 8.69 (m, 1H, pyridine) , 8.40 (m, 1H, pyridine), 8.59 (s, 1H, thiazole), 8.50 (s , 1H, thiazole), 8.30 (d, *J* = 7.5 Hz, 2H, phenyl), 7.85 (d, *J* = 7.5 Hz, 2H, phenyl), 7.57 (m, 1H, pyridine) , 7.51-7.60 (m , 5H, phenyl).
^{13}C NMR (100 MHz, $CDCl_3$) : δ 170.54 , 154.32 , 153.21, 152.62, 148.36, 147.69 , 143.25, 134.87, 133.35 , 133.54 , 133.20, 129.87, 127.29, 128.87 , 128.36, 128.24, 124.54, 115.51, 110.21.

4-(4-fluorophenyl)-2-(4-(2-pyridin-3-yl)thiazol-4-yl)phenyl)thiazole (j)
Yield 60% , Yellow , M.P. 228 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 9.25 (m, 1H, pyridine), 8.79 (m, 1H, pyridine) , 8.59 (s, 1H, thiazole), 8.55 (s , 1H, thiazole), 8.39 (m, 1H, pyridine), 8.36 (d, *J* = 7.5 Hz, 2H, phenyl), 8.15 (m, 2H, phenyl) , 7.85 (d, *J* = 7.5 Hz, 2H, phenyl), 7.57 (m, 1H, pyridine) , 7.30 (m , 2H, phenyl).

^{13}C NMR (100 MHz, $CDCl_3$) : δ 170.84, 162.95 ,154.23, 153.56, 152.36, 148.95, 147.35, 143.32, 134.45, 133.32, 133.21, 130.62, 128.96, 128.54, 128.41, 124.32,116.32,115.21, 110.21.

4-(4-chlorophenyl)-2-(4-(2-pyridin-3-yl)thiazol-4-yl)phenyl)thiazole (k)
Yield 65% , Yellow , M.P. 174 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 9.24 (m, 1H, pyridine), 8.75 (m, 1H, pyridine) , 8.69 (s, 1H, thiazole), 8.51 (s , 1H, thiazole) , 8.46 (m, 1H, pyridine), 8.29 (d, *J* = 7.5 Hz, 2H, phenyl), 7.85 (d, *J* = 7.5 Hz, 2H, phenyl), 7.57 (m, 1H, pyridine) , 7.41-7.98 (m , 4H, phenyl).
^{13}C NMR (100 MHz, $CDCl_3$) : δ 170.47, 163.56 ,154.58, 153.21, 152.47, 149.01, 146.47, 142.32, 136.75, 134.48 , 133.47, 131.66, 129, 128.99, 128.00, 124.12,116.87,115.27, 110.47.

4-(4-bromophenyl)-2-(4-(2-pyridin-3-yl)thiazol-4-yl)phenyl)thiazole (l)
Yield 50% , Brown , M.P. 210 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 8.99 (m, 1H, pyridine), 8.88 (m, 1H, pyridine) , 8.60 (s, 1H, thiazole), 8.55 (s , 1H, thiazole) , 8.48 (m, 1H, pyridine) , 8.30 (d, *J* = 7.5 Hz, 2H, phenyl), ,7.89 (d, *J* = 7.5 Hz, 2H, phenyl), 7.78 (d , *J* = 8Hz, 2H , phenyl), 7.76 (d , *J* = 8Hz, 2H , phenyl), 7.57 (m, 1H, pyridine).
^{13}C NMR (100 MHz, $CDCl_3$) : δ 170.84, 162.95 ,154.23, 153.56, 152.36, 148.95, 147.35, 143.32, 134.45, 133.32, 133.21, 130.62, 128.96, 128.54, 128.41, 124.32,116.32,115.21, 110.21.

2-(pyridin-3-yl)-4-(4-(4-(p-tolyl)thiazol-2-yl)phenyl)thiazole (m)
Yield 70% , White , M.P. 199-202 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 9.11 (m, 1H, pyridine), 8.85 (m, 1H, pyridine) , 8.62 (s, 1H, thiazole), 8.51 (s , 1H, thiazole), 8.46 (m, 1H, pyridine), 8.29 (d, *J* = 7.5 Hz, 2H, phenyl), ,7.85 (d, *J* = 7.5 Hz, 2H, phenyl), 7.67 (d , *J* = 8Hz, 2H , phenyl), 7.57 (m, 1H, pyridine) , 7.29 (d , *J* = 8Hz, 2H , phenyl), 2.34 (s,3H, methyl).
^{13}C NMR (100 MHz, $CDCl_3$) : δ 170.84, 162.95 ,154.23, 153.56, 152.36, 148.95, 147.35, 143.32, 134.45, 133.32, 133.21, 130.62, 128.96, 128.54, 128.41, 124.32,116.32,115.21, 110.21, 21.35.

4-(4-methoxyphenyl)-2-(4-(2-(pyridin-3-yl)thiazol-4-yl)phenyl)thiazole (n)
Yield 62% , Yellow , M.P. 198 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 8.95 (m, 1H, pyridine), 8.79 (m, 1H, pyridine) , 8.69 (s, 1H, thiazole), 8.55 (s , 1H, thiazole) , 8.45 (m, 1H, pyridine), 8.29 (d, *J* = 7.5 Hz, 2H, phenyl), 7.85 (d, *J* = 7.5 Hz, 2H, phenyl), 7.57 (m, 1H, pyridine) , 7.55 (d , *J* = 8Hz, 2H , phenyl), 7.09 (d , *J* = 8Hz, 2H , phenyl), 3.83 (s, 3H, methoxy).
^{13}C NMR (100 MHz, $CDCl_3$) : δ 170.84, 162.95 ,154.23, 153.56, 152.36, 148.95, 147.35, 143.32, 134.45, 133.32, 133.21, 130.62, 128.96, 128.54, 128.41, 124.32,116.32,115.21, 110.21, 55.85.

4-(4-nitrophenyl)-2-(4-(2-(pyridin-3-yl)thiazol-4-yl)phenyl)thiazole (o)
Yield 65% , Yellow , M.P. 196 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 9.22 (m, 1H, pyridine), 8.75 (m, 1H, pyridine) , 8.46 (m, 1H, pyridine), 8.69 (s, 1H, thiazole), 8.55 (s , 1H, thiazole), 8.29 (d, *J* = 7.5 Hz, 2H, phenyl), ,7.85 (d, *J* = 7.5 Hz, 2H, phenyl), 7.57 (m, 1H, pyridine) , 7.55 (d , *J* = 8Hz, 2H , phenyl), 7.09 (d , *J* = 8Hz, 2H , phenyl).
^{13}C NMR (100 MHz, $CDCl_3$) : δ 170.84, 162.95 ,154.23, 153.56, 152.36, 148.95, 147.35, 143.32, 134.45, 133.32, 133.21, 130.62, 128.96, 128.54, 128.41, 124.32,116.32,115.21, 110.21 .

4-(2-(4-(2-(pyridin-3-yl)thiazol-4-yl)phenyl)thiazol-4-yl)benzonitrile (p)
Yield 62% , Yellow , M.P. 234 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 9.32 (m, 1H, pyridine), 8.75 (m, 1H, pyridine) , 8.46 (m, 1H, pyridine), 8.69 (s, 1H, thiazole), 8.55 (s , 1H, thiazole), 8.29 (d, *J* = 7.5 Hz, 2H, phenyl), ,7.85 (d, *J* = 7.5 Hz, 2H, phenyl), 7.57 (m, 1H, pyridine) , 7.97 (d , *J* = 8Hz, 2H , phenyl), 7.82 (d , *J* = 8Hz, 2H , phenyl).
^{13}C NMR (100 MHz, $CDCl_3$) : δ 170.84, 154.91, 153.21, 152.34, 148.74 , 147.92, 143.37, 137.31, 134.24, 133.47, 133.52 , 132.45, 128.45, 128.32, 124.87,126.32 , 118.63 , 112.54 , 111.52 ,110.51.

4-phenyl-2-(4-(2-pyridin-4-yl)thiazol-4-yl)phenyl)thiazole (q)
Yield 75% ,Yellow , M.P. 220-224 ^{0}C.^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57-7.8(m, 5H, phenyl), 7.89 (s,1H, thiazole), 7.04(d, *J* =7.7Hz, 2H, Pyridine), 8.01-8.34 (m, 4H, Phenyl), 8.1(s,1H, thiazole), 8.76 (d, *J* =7.1 Hz, 2H, pyridine).
^{13}C NMR (100 MHz, $CDCl_3$): 166.14, 164.38, 146.11, 138.83, 133.13, 131.80, 130.40, 128.12, 127.01, 126.76, 122.51, 120.10, 117.32, 115.45, 114.23, 113.78, 112.12

4-(4-fluorophenyl)-2-(4-(2-(pyridin-4-yl)thiazol-4-yl)phenyl)thiazole (r)
Yield 78% , Yellow , M.P. 252 ^{0}C.^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (dd, *J* = 11 and 8 Hz, 2H, phenyl), 7.9 (s, 1H, thiazole), 7.98 (d, *J* = 7.7 Hz, 2H, Pyridine), 8.1 (dd, *J* = 8 and 2 Hz, 2H, phenyl), 8.01-8.02 (m, 4H, Phenyl), 8.33 (s, 1H, thiazole) , 8.76 (d, *J* = 7.7 Hz, 2H, Pyridine)

^{13}C NMR (100 MHz , $CDCl_3$): δ 166.14, 164.38, 162.03, 160.15, 150.11, 147.14, 142.17, 140.87, 139.83, 135.13, 132.80, 128.01, 126.76, 126.50, 120.10, 117.32, 115.45, 115.23, 113.78, 112.12.

4-(4-chlorophenyl)-2-(4-(2-(pyridin-4-yl)thiazol-4-yl)phenyl)thiazole (s)
Yield 80% , Yellow , M.P. 198 ^{0}C.^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 7.6Hz, 2H, Phenyl), 7.54 (d, *J* = 7.6Hz, 2H, phenyl), 7.26 (s, 1H,thiazole), 7.32 (d, *J* = 7.7Hz, 2H, Pyridine), 8.01-8.05 (m, 4H, Phenyl), 8.78 (s, 1H, thiazole), 8.12 (d, *J* = 7.7Hz, 2H, Pyridine)
^{13}C NMR (100MHz, $CDCl_3$): δ 166.14, 163.38, 154.14, 142.83, 136.13, 132.80, 131.20, 129.09, 128.01, 127.76, 122.51, 120.10, 117.12, 115.45, 114.23, 112.78, 110.12.

4-(4-bromophenyl)-2-(4-(2-(pyridin-4-yl)thiazol-4-yl)phenyl)thiazole (t)
Yield 62% , Yellow , M.P. 220-222 ^{0}C.^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 7.8Hz, 2H, phenyl), 7.12 (d, *J* = 7.8Hz, 2H, phenyl), 7.46 (s, 1H, thiazole), 8.0 (d, *J* = 7.7Hz, 2H, Pyridine), 8.01-8.04 (m, 4H, Phenyl), 7.99 (s, 1H, thiazole), 8.46 (d, *J* = 7.7Hz, 2H, Pyridine)
^{13}C NMR (100MHz, $CDCl_3$): δ 166.14, 162.38, 157.11, 154.83, 149.13, 146.80, 139.40, 135.12, 134.01, 131.76, 129.51, 126.10, 120.32, 117.45, 116.23, 114.78, 112.12.

2-(pyridin-4-yl)-4-(4-(4-(p-tolyl)thiazol-2-yl)phenyl)thiazole (u)
Yield 76% , Yellow , M.P. 218-220 ^{0}C.^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (s, 3H, methyl), 6.99 (d, *J* = 7.4 Hz, 2H, phenyl), 7.89 (d, *J* = 7.4 Hz, 2H, phenyl), 7.57(d, *J* = 7.7Hz, 2H, Pyridine), 8.01 (s, 1H), 8.01-8.03 (m, 4H, Phenyl), 8.07 (s, 1H), 8.12 (d, *J* = 7.7Hz, 2H, Pyridine)
^{13}C NMR (100 MHz, $CDCl_3$): δ 165.14, 162.38, 157.11, 151.83, 145.13, 141.80, 139.40, 136.12, 132.01, 128.76, 126.51, 122.10, 122.32, 117.45, 115.23, 114.78, 112.12, 24.34(CH_3)

4-(4-methoxyphenyl)-2-(4-(2-(pyridin-4-yl)thiazol-4-yl)phenyl)thiazole (v)
Yield 80% , Brown , M.P. 224 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 3.76 (s, 3H, methoxy), 7.06 (d, *J* = 7.28 Hz, 2H, phenyl), 8.00 (d, *J* = 7.7Hz, 2H, Pyridine), 7.41 (s, 1H, thiazole), 8.01-8.04 (m, 4H, Phenyl), 8.75 (d, *J* = 7.28 Hz, 2H, phenyl), 8.56 (s, 1H, thiazole), 8.87 (d, *J* = 7.7Hz, 2H, Pyridine); ^{13}C NMR (400MHz , $CDCl_3$): δ 165.14, 164.38, 159.11, 154.83, 149.13, 147.80, 142.40, 139.12, 135.01, 132.76, 131.51, 128.10, 122.32, 120.45, 119.23, 115.78, 112.12, 62.10.

4-(4-nitrophenyl)-2-(4-(2-(pyridin-4-yl)thiazol-4-yl)phenyl)thiazole (w)
Yield 78% , Brown , M.P. 212 ^{0}C.^{1}H NMR (400MHz, $CDCl_3$): δ 7.49 (d, *J* = 7.9 Hz, 2H, phenyl), 7.06 (d, *J* = 7.7Hz, 2H, Pyridine), 7.98 (s, 1H, thiazole), 8.01-8.04 (m, 4H, Phenyl), 7.98 (d, *J* = 7.9 Hz, 2H, phenyl), 7.99 (s, 1H, thiazole), 8.05 (d, *J* = 7.7Hz, 2H, Pyridine)
^{13}C NMR (100 MHz, $CDCl_3$): δ 165.14, 161.38, 156.11, 151.83, 149.13, 145.80, 142.40, 135.12, 132.01, 130.76, 128.51, 126.10, 122.32, 119.45, 116.23, 114.78, 111.12

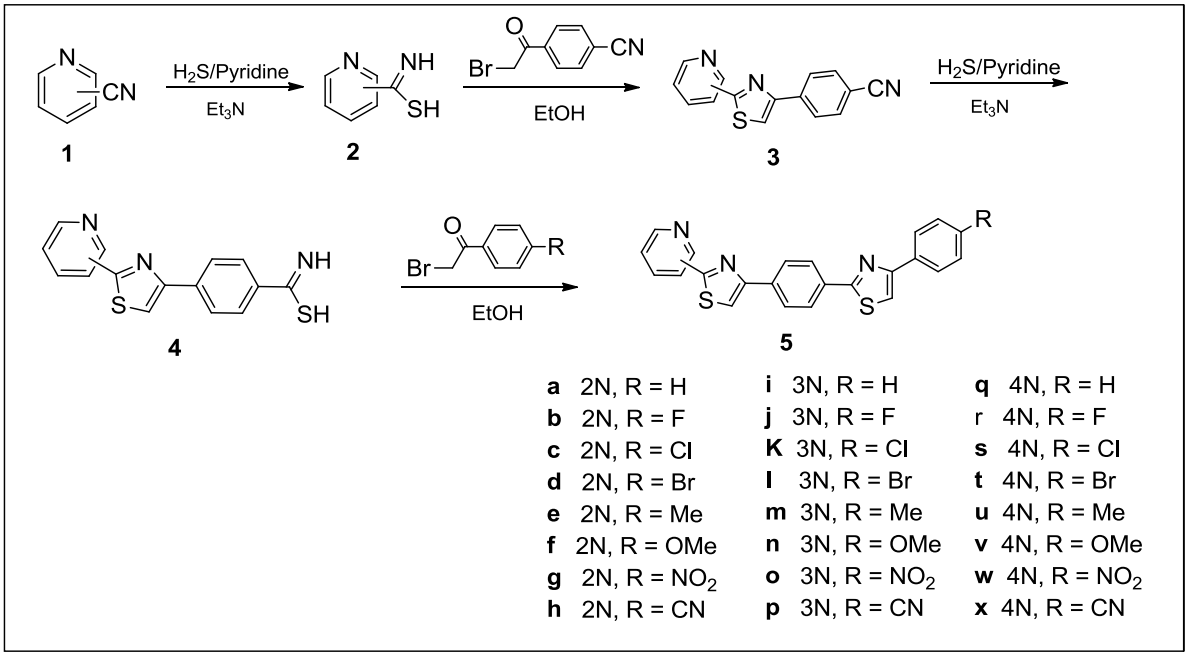
4-(2-(4-(2-(pyridin-4-yl)thiazol-4-yl)phenyl)thiazol-4-yl) benzonitrile (x)
Yield 66% , Yellow , M.P. 210-215 ^{0}C.^{1}H NMR (400MHz ,$CDCl_3$): δ 7.98 (d, *J* = 7.8 Hz, 2H, phenyl), 7.13 (d, *J* = 7.7Hz, 2H, Pyridine), 7.48 (s, 1H, thiazole), 8.04 (d, *J* = 7.8 Hz, 2H, phenyl), 8.01-8.34 (m, 4H, Phenyl), 8.75 (s, 1H, thiazole), 8.14 (d, *J* = 7.7Hz, 2H, Pyridine).
^{13}C NMR (100MHz, $CDCl_3$): δ 168.14, 161.38, 157.11, 148.83, 142.13, 131.80, 129.40, 126.12, 125.01, 122.76, 121.51, 119.10, 118.32, 115.45, 115.23, 113.78, 112.12

3. DISCUSSION:

3.1 Chemistry

According to **Scheme 1**, three isomeric pyridine nitriles **1** was treated with H_2S gas in pyridine and TEA to obtain the corresponding pyridine - carbothioimidic acid **2**. Compound **2** was then reacted with 4-cyano phenacyl bromide in ethanol to obtain isomeric 2-pyridyl- thiazol-4-yl-benzonitriles **3** . The above synthetic sequence steps are repeated to obtain the target compounds **5**. This two successive series of Hantzsch Thiazole results into formation of twenty four isomeric derivatives, **a to x** .The formation of the final product was ascertained by spectroscopic analysis. The structure of intermediate compound (**3**) for 4-pyridyl isomer was established by its ^{1}H NMR (**spectrum 1**) which showed two doublets at δ 7.8 and δ 8.72 of pyridine ring, integrating for two protons each. The thiazole ring proton appeared as singlet at δ 7.76. The protons of the cyano-substituted aromatic ring revealed two doublets at δ 7.74 and δ 8.13 integrating for two protons each. The ^{1}H NMR spectrum (**spectrum 2**) of **a** showed proton signals of pyridine ring at δ 8.64 integrating for one proton and δ 8.3 ,7.98 , 8.26 integrating for three protons, respectively. The aromatic protons (4H) appeared as doublet of a doublet at δ 8.01-8.02. The thiazole ring protons appeared as singlets

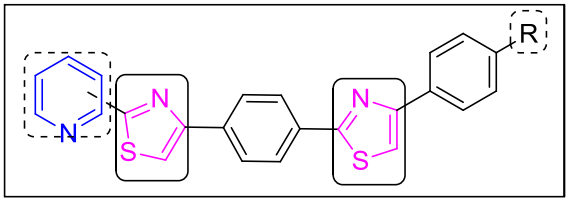
at δ 8.26 and δ 8.05. The other substituted aromatic protons appeared as multiplet at δ 7.48 and doublet at δ 8.05. The ^{13}C NMR (**spectrum 3**) of **a** showed in all a total 19 signals for 19 carbon atoms. The ^{1}H NMR spectrum (**spectrum 4**) of **e** showed proton signals of pyridine ring at δ 8.72 integrating for one protons and δ 8.3 ,7.61 , 8.26 integrating for three protons respectively. The aromatic protons (4H) appeared as doublet of a doublet at δ 8.1-8.25. The thiazole ring protons apeeared as singlet at δ 8.6 and δ 7.95. The other substituted phenyl protons appeared as doublet at δ 7.48 and doublet at δ 7.61. The representative ^{1}H NMR spectrum (**spectrum 5**) of **r** showed two doublets at δ 7.98 and δ 8.76 of pyridine ring, integrating for two protons each. The aromatic protons (4H) appeared as doublet at δ 8.01-8.02. The thiazole protons of two rings appeared as singlets at δ 7.9 and δ 8.33. The protons of the substituted aromatic ring revealed two doublet of doublets at δ 7.24 and δ 8.1 for two protons each, due to coupling with fluorine. The ^{13}C NMR (**spectrum 6**) showed in all a total 20 signals for 17 carbon atoms. The three extra signals are observed due to the presence of F atom. The ipso, ortho and the meta carbon on the ring showed couplings with F with *J* values of 224 Hz, 22 Hz and 3Hz respectively. The structure of all other derivatives was confirmed similarly from their respective ^{1}H NMR and ^{13}C NMR data.



Scheme 1 : Hantzsch Thiazole synthesis

3.2 Pharamacokinetic properties: Prediction of bioactivity score using Lipinski Rule of five (RO5):

The synthesized derivatives have three aromatic rings in their structures viz.4-substituted phenyl, thiazole and positional isomeric pyridine rings.



Based on structural diversity of the molecules, it is technically difficult to screen each one of them for in vitro activity against number of bacteria and fungi strains. Computational methods can provide filters for these derivatives and provide information about SAR. Drug solubility and permeability through lipid bi-layer of cell membrane is always an important issue for organic and medicinal chemist. The physico-chemical properties play a vital role in defining drug like molecule (DLM) character and pharmacokinetics properties such as absorption, distribution, metabolism, excretion and toxicity (ADMET) of a molecule. The necessary physico-chemical properties and their importance in the early drug discovery was explained by the works of Lipinski and others. These rules states that the molecule with molecular mass less than 500, Log P value less than 5, hydrogen bond donors less than 5, hydrogen bond acceptors less than 10, polar surface area less than 140 and the number of rotatable bonds less than 10 could be a molecule with DLM character. Molinspiration, an online toolkit, (http://www.molinspiration.com/cgi-bin/properties 2014) was used to calculate these physicochemical properties and the values are presented in **Table I**. Furthermore, each compound is in good agreement with Lipinski's rule of five and therefore show excellent drug like property. A molecule with not more than one Lipinski's violation, is likely to be developed as an orally active drug candidate. Almost all compounds followed the criteria for orally active drug and therefore, these compounds may have a good potential for eventual

development as oral agents. An overall drug-likeness was studied using molsoft online (www.molsoft.com) and from the data represented in **Table I**, most of these compounds showed good model score and therefore can be considered to possess good drug like properties.

Comp	Mol wt	HBA	HBD	Log P	Log S	TPSA	Mol vol	Drug likeliness	N Atom	nON	nOH NH	lipinski violation	Nrotb
a	397.07	5	0	5.84	-8.94	38.68	338.63	-0.95	28	3	0	1	4
b	415.06	5	0	6.00	-9.46	38.68	343.56	-0.61	29	3	0	1	4
c	431.03	5	0	6.51	-9.90	38.68	352.17	-0.46	29	3	0	1	4
d	474.98	5	0	6.65	-10.09	38.68	356.52	-0.79	29	3	0	1	4
e	411.09	5	0	6.29	-9.40	38.68	355.19	-0.88	29	3	0	1	4
f	427.08	6	0	5.89	-9.20	47.91	364.18	-0.48	30	4	0	1	5
g	443.06	7	1	5.80	-9.44	84.50	361.97	-0.74	31	6	0	1	5
h	422.07	6	0	5.59	-9.53	62.47	355.49	-0.97	30	4	0	1	4
I	397.07	5	0	5.91	-8.85	38.68	338.63	-0.22	28	3	0	1	4
j	415.06	5	0	6.08	-9.36	38.68	343.56	-0.01	29	3	0	1	4
k	431.03	5	0	6.59	-9.80	38.68	352.17	0.17	29	3	0	1	4
l	474.98	5	0	6.72	-10.00	38.68	356.52	-0.21	29	3	0	1	4
m	411.09	5	0	6.36	-9.30	38.68	355.19	-0.22	29	3	0	1	4
n	427.08	6	0	5.97	-9.11	47.91	364.18	-0.02	30	4	0	1	5
o	443.06	7	1	5.87	-9.34	84.50	361.97	-0.11	31	6	0	1	2
p	422.07	6	0	5.67	-9.44	62.47	355.49	-0.35	30	4	0	1	4
q	397.07	5	0	5.69	-9.22	38.68	338.63	-49	28	3	0	1	4
r	415.06	5	0	5.86	-9.73	38.68	343.56	-0.52	29	3	0	1	4
s	431.03	5	0	6.37	-10.18	38.68	363.61	-0.31	29	3	0	1	4
t	474.98	5	0	6.50	-10.37	38.68	356.52	-0.73	29	3	0	1	4
u	411.09	5	0	6.14	-9.67	38.68	355.19	-0.66	29	3	0	1	4
v	427.08	6	0	5.75	-9.48	47.91	364.18	-0.41	30	4	0	1	5
w	443.06	7	1	5.65	-9.71	84.50	361.97	-0.41	31	6	0	1	5
x	422.07	6	0	5.45	-9.81	62.47	355.49	-0.77	30	4	0	1	4

4. CONCLUSION:

In conclusion, a series of pyridyl-thiazole derivatives **(5 a-x)** were successfully synthesized and characterized by spectroscopic methods. Because of the concave structure of the designed molecule, it was envisaged that these molecules may have better binding capacities with the reactive site and also have better lipophilicity. The ring rigidity has been obtained because of heterocyclic aromatics ring in the structure and due to these the biological activity should enhance. However, for better understanding of the structure-activity relationship, further studies are warranted.

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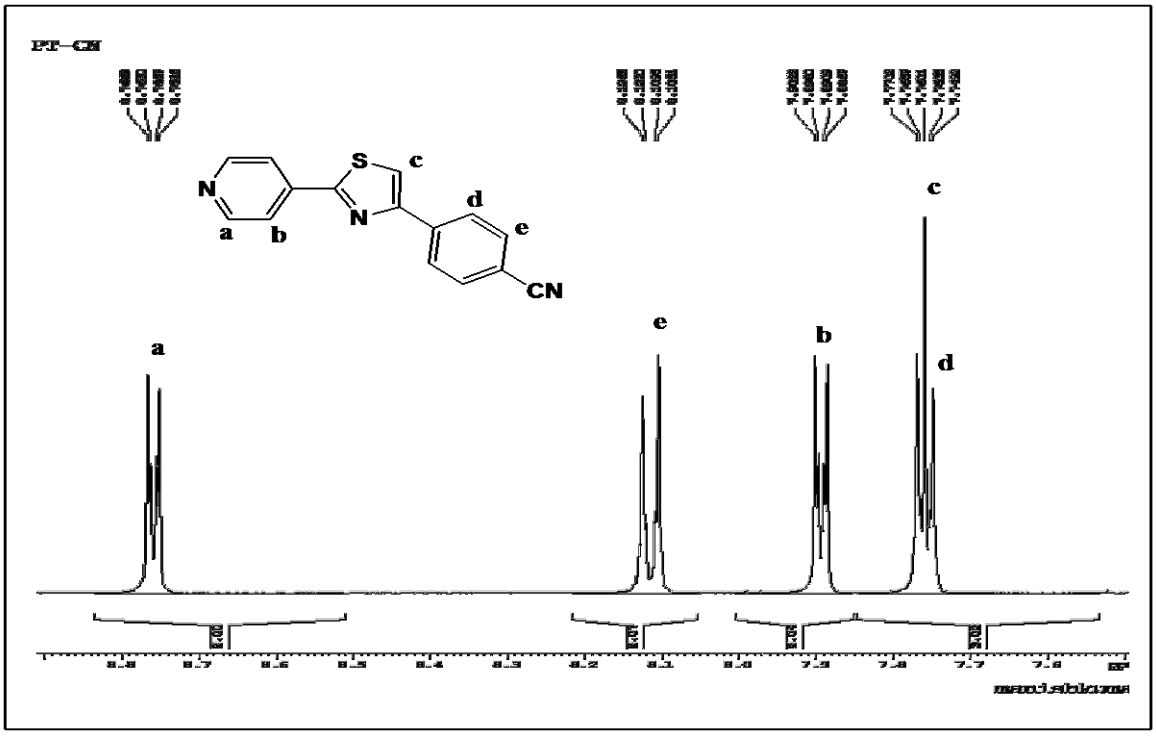
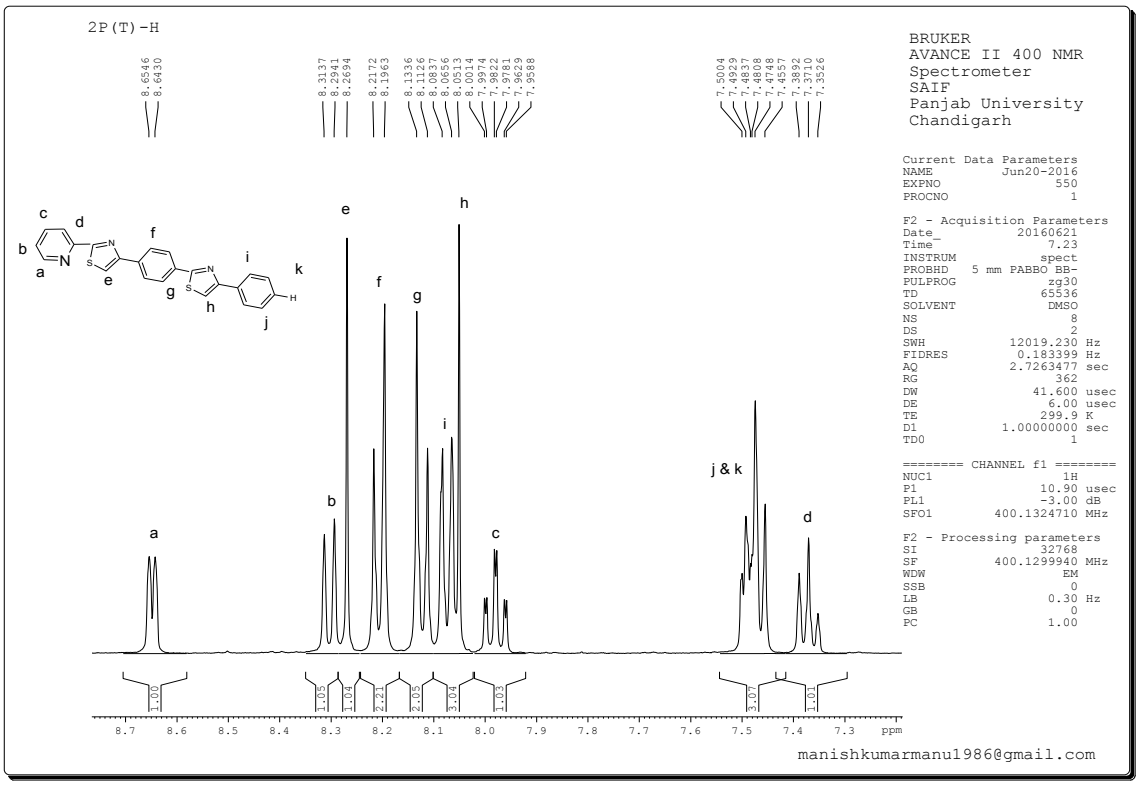
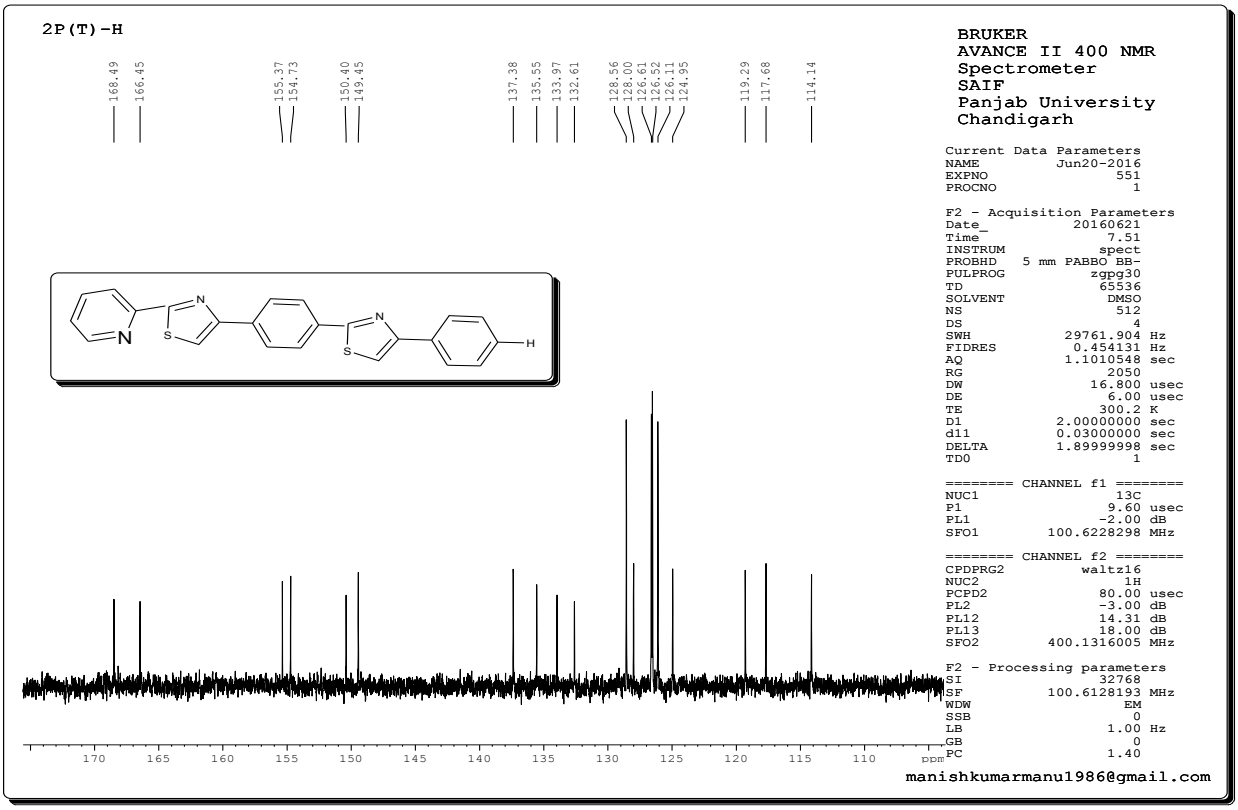


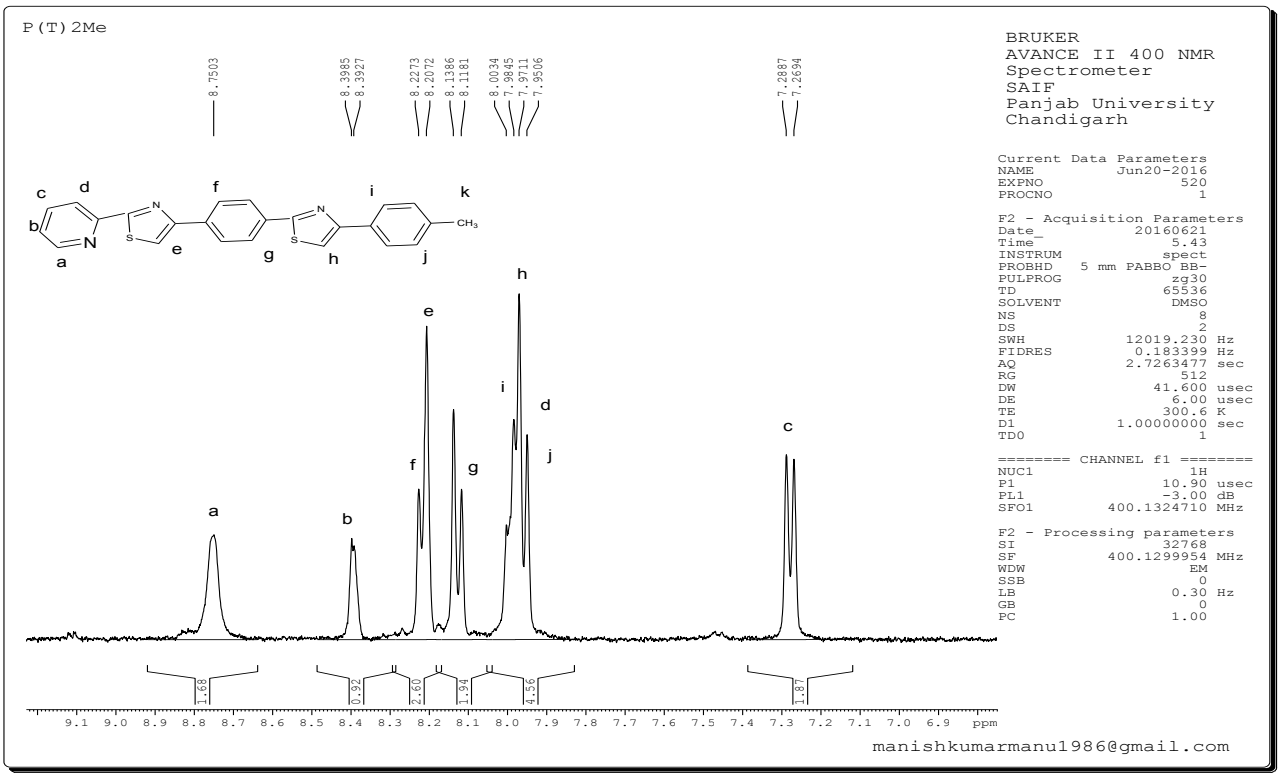
Spectrum 1 : The ^{1}H NMR spectrum of intermediate **3**



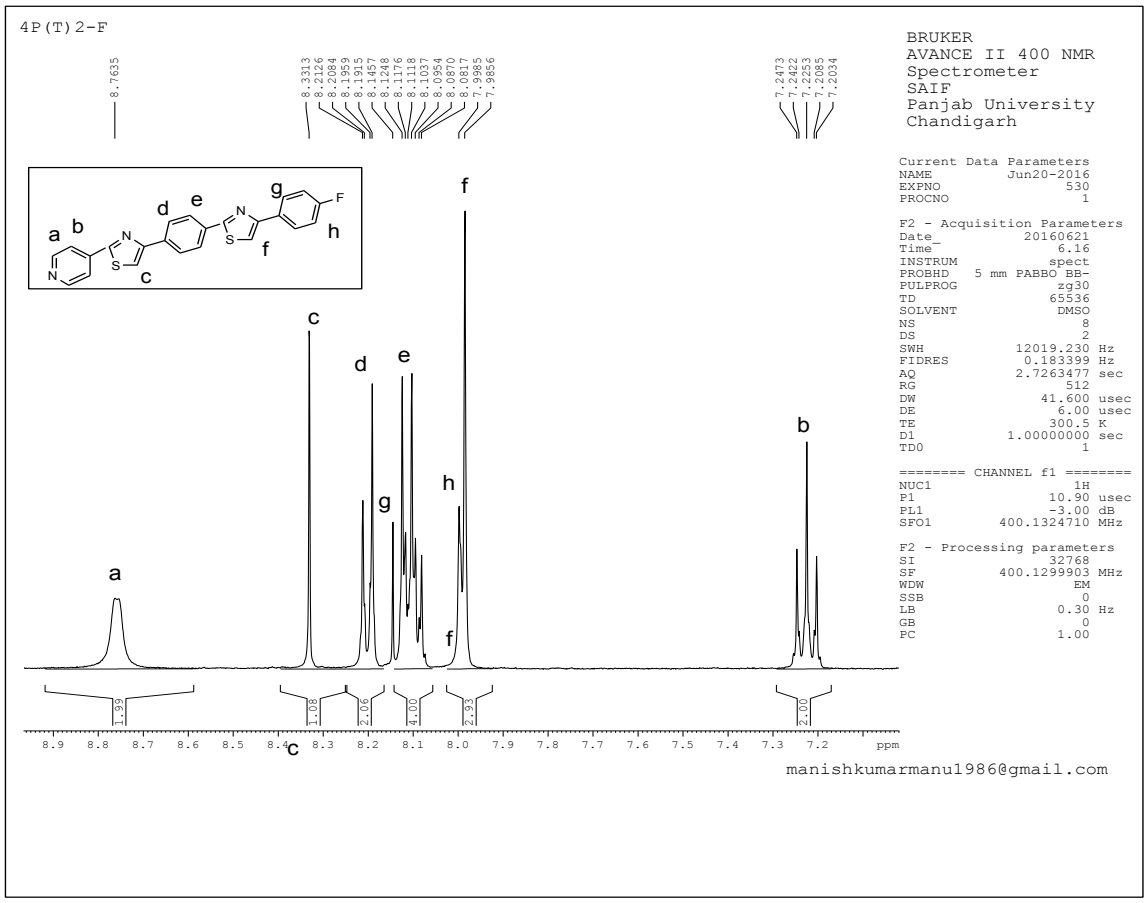
Spectrum 2 : The ^{1}H NMR spectrum of compound **a**



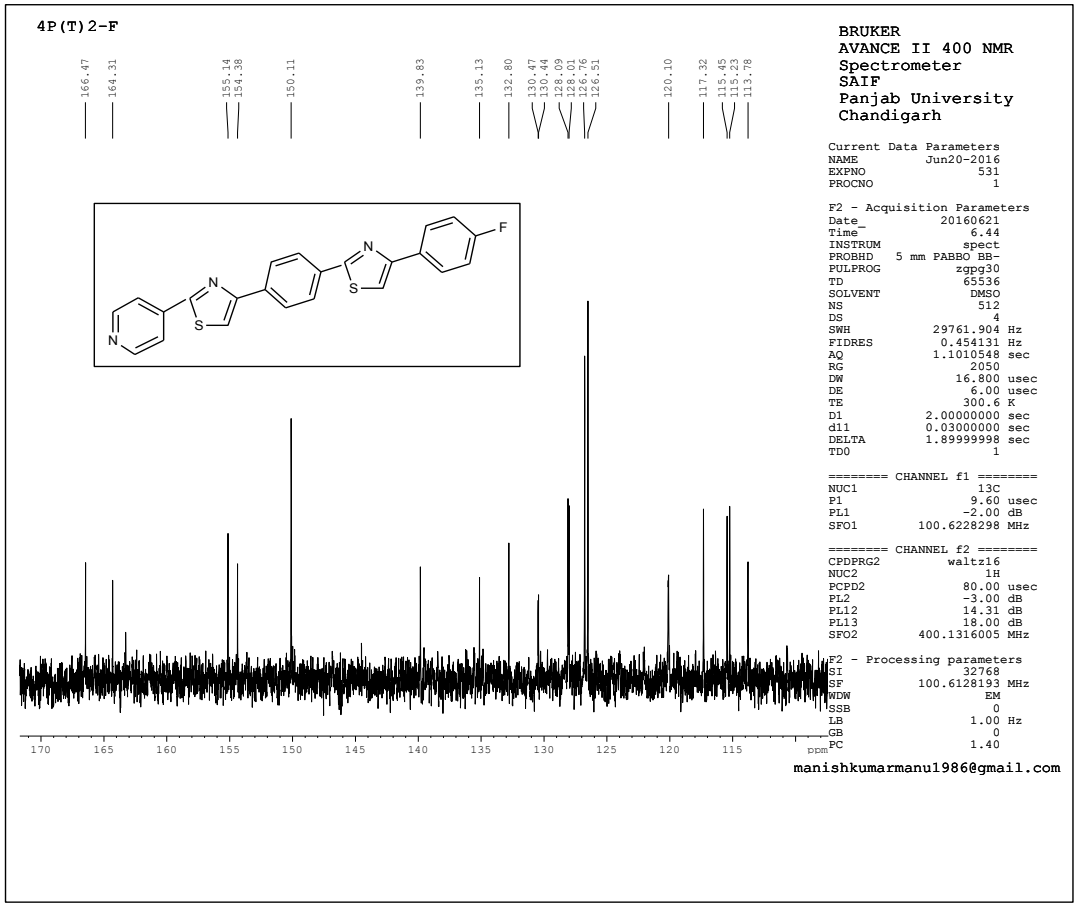
Spectrum 3 : The ^{13}C NMR spectrum of compound **a**



Spectrum 4 : The ^{1}H NMR spectrum of compound **e**



Spectrum 5 : The ^{1}H NMR spectrum of compound **r**



Spectrum 6 : The ^{13}C NMR spectrum of compound **r**

Synthesis, Characterisation and *In Vitro* Antibacterial Study of Coumarin-Indole Hydrazones

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Abstract: *A new series of Coumarin-Indole derivatives INDS, INDC, INDB and INDN were synthesized from 3-acetyl indole hydrazone and substituted salicylaldehyde. The structures of the synthesized compounds have been established on the basis of physical and spectral data. They shows a prominent absorption of -(C=N-) in FTIR and a common peak indolic -NH at 11.9 and 12.14 ppm in the form of singlet. A survey of existing literature revealed that there are no reports describing the synthesis of such hydrazones.*

Key Words: *Coumarin-Indole, indole hydrazone, salicylaldehyde, indolic -NH*

1. INTRODUCTION:

In the past few decades, the incidence of microbial infection has increased on frightening levels over the world as a result of antimicrobial resistance. Microbial infections are a growing problem in contemporary medicine and the use of antibiotics is common across the world. Consequently, there is an urgent need to widen new antimicrobial agents, which have a broad spectrum of activity against the resistant micro-organisms[1,2].

Many antibiotics including penicillin and streptomycin also contain heterocyclic ring system. Many pigments such as indigo, hemoglobin and anthrocynin are also heterocyclic compounds. Important drugs such as suphathiazol, pyrethrin, rotenine, cocaine, barbiturates also possess heterocyclic system. These compounds are also known to be used as starting material for the synthesis of new drugs. Synthetic method for obtaining heterocyclic compound may be divided into ring closure reaction, addition reaction and replacement reaction [3]. Coumarins are well known naturally occurring heterocyclic compounds isolated from various plants. They belong to class of flavanoid. Chemically, coumarins are lactones containing 1-benzopyran-2-one system. Coumarin derivatives have been reported for anti-coagulant, anti-inflammatory[4], anti-bacterial[5-14], anti-HIV, anti-oxidant[15], anti-allergic, anti-cancer[16] and ant-proliferative and antiviral[17] activities, like anti-inflammatory, anti-microbial, anti-tumour, anti-HIV, herbicidal, fungicidal[18] and CNS stimulant[19] activities.

Indole is an important heterocyclic system because it is built into proteins in the form of amino acid tryptophan, because it is the basis of drugs like indomethacin and because it provides the skeleton of indole alkaloids biologically active compounds from plants including strychnine and LSD. The incorporation of indole nucleus, a biologically accepted pharmacophore in medicinal compounds, has made it versatile heterocyclic possessing wide spectrum of biological activities. The indole ring system represent one of the most abundant and important heterocycles in nature found in a hugely diverse array of biologically significant natural compounds from simple derivatives such as the neurotransmitter serotonine to complex alkaloid such as the clinically used anticancer agents vinblastine and mitocyne C, and the antihypertensive alkaloid reserpine[20].

Motivated from these observations, here we attempt to discover a new coumarin series with improved biological activity. We designed and synthesized some Coumarin-Indole derivatives INDH, INDS, INDC, INDB and INDN (Scheme 1) and anti-bacterial activity of the newly synthesized compounds and a reference drug (amoxicillin) was evaluated.

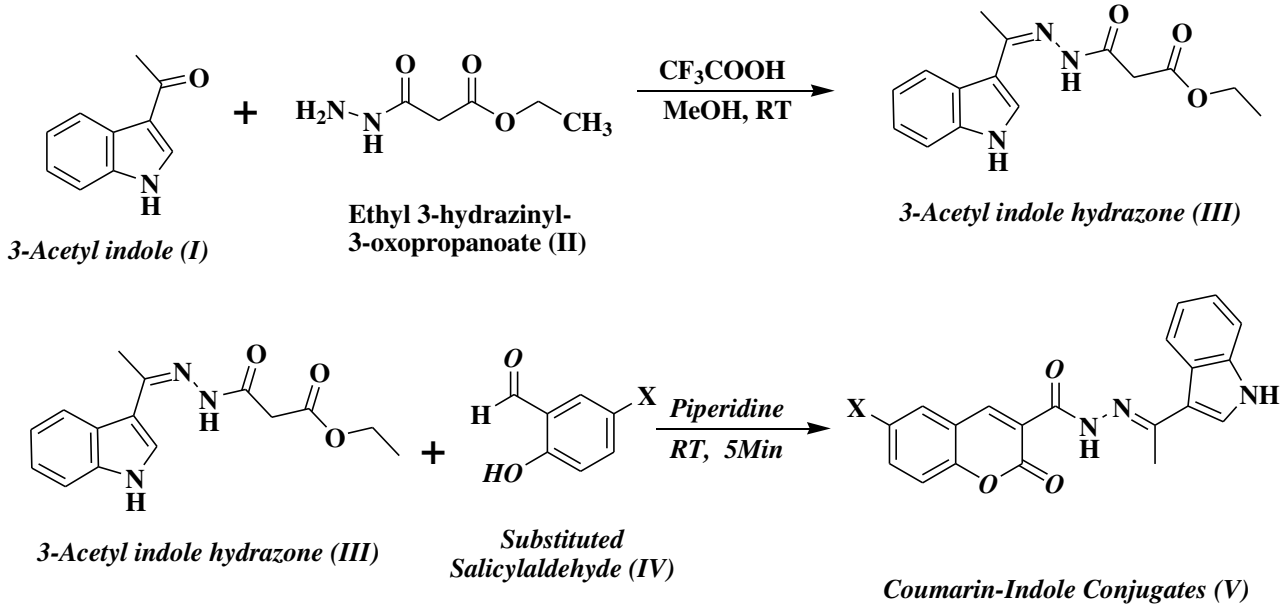
2. MATERIALS:

Solvents for synthesis were reagent grade and used as obtained. The starting materials such as ethyl 3-hydrazinyl-3-oxopropanoate, 3-acetyl indole, 5-bromo salicylaldehyde, 5-chloro salicylaldehyde, 5-nitrosalicylaldehyde were obtained from Sigma-Aldrich, India. Salicylaldehyde, Triflouro acetic acid, Piperidine, acetone, methanol, ethanol and dichloromethane were obtained from SD-FCL Chemical Limited, Mumbai, India. All compounds were routinely checked by TLC on silica gel G plates using petroleum ether/ethyl acetate (7:3; 6:4; 5:5 by V/V) as solvent system and the developed plates were visualized by UV light and iodine vapours.

3. METHOD:

The target Coumarin-indole derivatives were synthesized in two steps (Scheme 1). Initially, 3-acetyl indole hydrazone (**III**) was prepared from ethyl 3-hydrazinyl-3-oxopropanoate, 3-acetyl indole by reacting 3-acetyl indole (**I**) and ethyl 3-hydrazinyl-3-oxopropanoate (**II**). Subsequently, Coumarin-Indole derivatives (**V**) were obtained by reacting (**III**)

with corresponding salicylaldehyde (**IV**) in presence of few drops of piperidine followed by neutralization with dil. HCl (Scheme 1).



3-Acetyl indole (I)

Ethyl 3-hydrazinyl-3-oxopropanoate (II)

3-Acetyl indole hydrazone (III)

3-Acetyl indole hydrazone (III)

Substituted Salicylaldehyde (IV)

Coumarin-Indole Conjugates (V)

Scheme 1: Synthesis of Coumarin-Indole Conjugates

The *in vitro* antibacerial activity was performed according to procedure explained by Arpit et al[21]. A standardize inoculums were inoculated with the help of a sterile cotton swab on the surface of the agar plate. Disc of antimicrobial agents were placed on the surface of agar plate. The plates were incubated at 37°C for 24 hours and susceptibility is determined on the basis of zone of inhibition. A standard and control strain was also tested for comparison. The diameter of the zone of growth inhibition around each disc were measured and compared with zones of inhibition of standard and control.

3. RESULTS AND DISCUSSION:

Melting points of the synthesized compounds were determined with open capillary tube on a VEEGO melting point apparatus and are uncorrected. The H^1-NMR spectra were obtained on a 600 MHz from SPPU, Pune. IR spectra were recorded by "FT-IR Jasco" spectrometer at our centre.

The structures of the synthesized compounds have been established on the basis of physical and spectral data. They shows a prominent absorption of -(C=N-) in FTIR. It also shows a common peak indolic -NH at 11.9 and 12.14 ppm in the form of singlet. The detailed physical and spectral properties are as follow-

1) Ethyl 2-(1-(1H-indol-3-yl)ethylideneaminocarbamoyl)acetate (**INDH**)**: 185-186°C, White, 85%, FTIR(cm^{-1})**: 3181.97(NH) 1712.33 (ester) 1660(C=O) 1181.91(C-O) 1317(N-N) 1500-1600(arom), **H^1-NMR** (*d-DMSO*) (δ, ppm,): 11.4(1H, s), 11.9(1H, s), 8.1(1H, s), 1.22(3H, s), 3.5 (2H, s), 8.8 (1H, dd), 7.2(1H, ddd), 7.4 (1H, dd), 7.46 (1H, ddd), 4.1(2H, q), 1.3(3H, t).

2) (14E)-N'-(1-(1H-indol-3-yl)ethylidene)-2-oxo-2H-chromene-3-carbohydrazide (**INDS**)**: 160-164°C, White, 40%, FTIR(cm^{-1})**: 3166.5 (NH) 1704 (lactone ring) 1611.10(CO) 1500-1600 (aromatic) 1150 (C-O stretching), **H^1-NMR**(d-DMSO) (δ, ppm,): 2.5(3H, s), 7.4(2H, t), 12.00(1H, s), 11.6(1H, s), 7.6(2H, t), 9.1(1H, s), 8.1(1H, dd), 8.6 (1H, m), 8.2 (1H m), 7.6(1H m).

3) (14E)-N'-(1-(1H-indol-3-yl)ethylidene)-6-chloro-2-oxo-2H-chromene-3-carbohydrazide (**INDC**): **120-124°C, White, 54%, FTIR(cm^{-1}):** 3161.55 (N-H) 1176.44(N-N), 1610(CO), 937.55 (Cl), 1704.2 (CO), 1500-1600 (arom), **H^1-NMR**(*d-DMSO*) (δ,ppm,): 11.5I(1H, s), 11.7(1H, s), 8.2(2H, d) 7.4(1H, d), 7.8(1H, dt), 7.6(1H, m), 7.4(1H, mm), 2.5(3H, s), 7.3 (1H, s), 6.96 (1H, d), 7.1(1H d).

4) (14E)-N'-(1-(1H-indol-3-yl)ethylidene)-6-bromo-2-oxo-2H-chromene-3-carbohydrazide (**INDB**): **154-158°C, Yellow, 89%, FTIR(cm^{-1}):** 1176.67(c-o stretching), 3155.93(N-H), 1611(C=O), 931.45(N-N), 1500-1600 (aromatic), 750.33 Br stretching , **H^1-NMR** (*d-DMSO*) (δ, ppm,): 11.9(1H, s, NH), 11.5 (1H, s NH), 7.2(3H, s), 8.3(2H, d), 8.1(1H, t), 7.57.2(3H, d), 5.50(3H, s).

5) (14E)-N'-(1-(1H-indol-3-yl)ethylidene)-6-nitro-2-oxo-2H-chromene-3-carbohydrazide (**INDN**): **156-160°C, Orange, 58%, FTIR(cm^{-1}):** 3121.22(NH), 1416.2-1341.25(NO_2), 1661.8(CO), 1725.66(lactone ring), 750.33(ortho coupling), 1500-1600(aromatic), 1150(C-O), **H^1-NMR** (*d-DMSO*) (δ, ppm): 2.6(3H, s), 12.0(1H, s) 11.6(1H, s) 7.3(1H, s), 7.2(1H, m), 7.6(1H, m), 7.8(1H. m), 7.4(1H, m), 8.6 (1H, s), 8.8(1H, dd), 7.2(1H, d).

Antibacterial Discussion: The compounds were serially diluted and different dilutions were tested against three organisms such as *Staphylococcus aureus, E. coli* and *Pseudomonas aeroginosa*. Out of the four tested compounds three compounds such as INDS, INDC and INDN a good activity against both Gram positive and Gram negative bacteria where as compounds INDB didn't exhibit any antibacterial activity. Amoxicillin (25 $\mu g/mL^{-1}$) was used as standard which showed a zone of inhibition of 8mm. Among the two Gram negative strains the compounds were found to be more effective against *P. aeroginosa* than *E. coli*. However if antibacterial activity is to be compared between Gram positive and Gram negative bacterial, the results are more promising against Gram positive organisms. The disc diffusion method was used for determining the antibacterial activity of the compounds and the results obtained were summarized in following table-1.

Organisms	*Conc.* ($\mu g/mL^{-1}$)	INDS	INDC	INDB	INDN
Staphylococcos aureus	25	-	-	No Activity	-
	50	6	7		-
	75	7	7		6
	100	9	12		7
	125	10	10		8
	150	12	14		9
E. Coli	No Activity	No Activity	No Activity		No Activity
Pseudomonas aeroginosa	25	-	-		-
	50	5	6		-
	75	5	7		6
	100	6	9		6
	125	7	10		7
	150	8	12		8

Table-1: Results of Antibacterial Activity

The results clearly indicate that the compounds have selective action on Gram negative organisms. The basic difference between Gram positive and Gram negative organism lies in organization. The compounds seem to interfere or inhibit the cell wall organization or maybe they do not allow the synthesis of cell wall or one of its components in Gram positive bacteria. Also the zone of inhibition seen around the antibiotic disc seems to increase in diameter with the increase in concentration of the drug.

4. CONCLUSION:

We reported the synthesis and structural characterization of four Coumarin-Indole hydrazones. Only three compounds show effective antibacterial activity where as INDB is inactive against Gram +ve and Gram –ve bacteria. All the synthesized compounds are moderately active when compared with standard Amoxicillin. The Minimum Inhibitory Concentration (MIC) of INDS and INDC is 50 $\mu g \cdot mL^{-1}$ for Gram +ve and Gram –ve bacteria whereas The Minimum Inhibitory Concentration (MIC) of INDN is 75 $\mu g \cdot mL^{-1}$ for both Gram +ve and Gram –ve bacteria. Since the compounds show activity against both Gram +ve and –ve bacteria, all the compounds can be screened for other enteric organisms which are known pathogens like *Salmonella, Pseudomonas, Vibrio* etc. Also Antifungal, Antiviral, Cytotoxic and anti-inflammatory activities can also be carried out.

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Synthesis Of Novel Pyrazole Containing Thiopyrimidine Derivatives

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Abstract: *A new series of pyrazole containing thiopyrimidine derivatives was synthesized hereby the condensation of chalcones with thiourea in ethanol as a reaction solvent.*

Keywords: *Chalcones, pyrazole, Thiopyrimidine derivatives.*

1. INTRODUCTION:

Pyrimidine rings have played an important role in medicinal chemistry, serving as key templates central to the development of numerous important therapeutic agents. Pyrimidine derivatives have found application in a wide range of medicinal chemistry because of their diverse biological activities as well as Pyrimidine nucleus exhibited remarkable pharmacological activities. The 4-aryl-1, 2, 3, 4-tetrahydropyrimidines has been given the name *Biginelli* compounds. The main interest in Biginelli compounds however is due to the strong antihypertensive activity exhibited by certain derivatives. Also a large number of substituted pyrimidines have been maintained to have several biological activities. Literature of survey indicates that the compounds having pyrimidine nucleus have wide range of therapeutic uses that include anti-inflammatory, antibacterial, anticancer, antiviral, anti HIV, antimalarial, antihypertensive, sedatives and hypnotics, anticonvulsant and antihistaminic[1-16]. Due to interesting activity of various substituted pyrimidine as biological agents, considerable attention has focused on this class. One of the methods for the synthesis of such compound is from α-β unsaturated carbonyl compound by the cyclization with thiourea to form the thiopyrimidine nucleus.

2. MATERIAL AND METHOD:

Melting points were uncorrected and determined in an open capillary tube. IR spectra were recorded on FTIR Shimadzu spectrometer. ^{1}H NMR spectra were recorded in DMSO-d_6 on Avance 300 MHz spectrometer using TMS as an internal standard. The mass spectra were recorded on EI-Shimadzu-GC-MS spectrometer. Elemental analyses were performed on a Carlo Erba 106 Perkin-Elmer model 240 analyzer.

3. DISCUSSION:

General Procedure For The Synthesis Of Pyrazole Containing Thiopyrimidine Derivatives

Preparation of 6(5-Chloro-2-hydroxyphenyl)-4-(5-chloro-3-methyl-1phenyl-1H-pyrazol-4-yl)-3, 4-dihydropyrimidine 2(1H)-thione. (11a)

A mixture of 5-Chloro-2-hydroxyphenyl-3-(5-chloro-3-methyl-1phenyl-1H-pyrazol-4yl) prop-2-en-1-one. (0.372 gm 1 mmol) and thiourea (99%) (0.100 gm 1mmol) in basic medium and ethanol as a reaction solvent was refluxed for 2 hours. After completion of the reaction (TLC), the reaction mixture was cooled at room temperature and poured in ice cold water (100 mL). The separated solid was filtered, washed and recrystallized from proper solvent.

The purity of synthesized thiopyrimidine was checked by TLC. Their structures were assigned by spectral analysis (IR, ^{1}H NMR, ^{13}CNMR and MS). Similarly, remaining compounds of this series were also prepared by same procedure. The physical data of synthesized compounds were tabulated as in Table 1

4. RESULTS AND DISCUSSION:

In continuation of our work on the synthesis of some new bioactive heterocyclic compounds[17-19] herein we report new series of pyrazolo containing thiopyrimidines in ethanol as a solvent **.**The starting chalcone is used by reported method [20] In order to optimize the reaction conditions, We found that ethanol as an efficient reaction medium in terms of reaction time as well as yields (92%). Encouraged by the results, we turned our attention to variety of substituted chalcones. In all cases, the reaction proceeded efficiently in high yields at 60°C using ethanol as reaction solvent.

5. ANALYSIS:

Spectroscopic data of selected compounds:

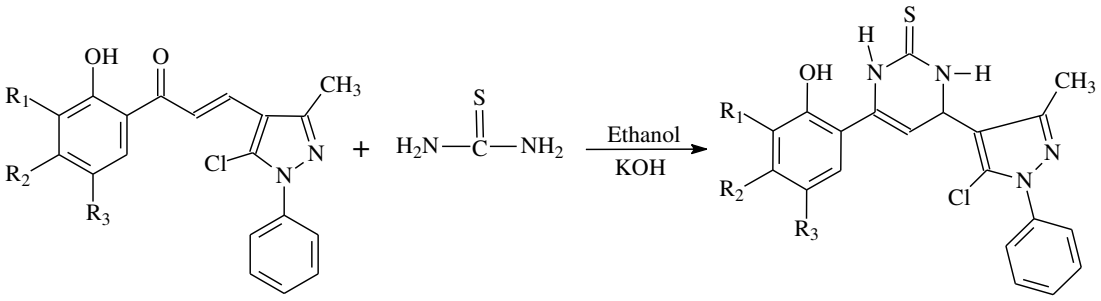
6(5-Chloro-2-hydroxyphenyl)-4-(5-chloro-3-methyl-1phenyl-1H-pyrazol-4-yl)-3, 4-dihydropyrimidine 2(1H)-thione. (11 b).

IR (KBr): 3777, 3418, 1632,1576,1425,750,687 cm^{-1}

^{1}H NMR (DMSO-d_6): δ1.9 (s, 3H, CH_3), 5.0 (s, 1H,-NH), 5.2 (s, 1H,-NH), 7.0-8.0 (m, 8H, Ar-H+ 5H of Thiopyrimidine), 8.5 (s, 1H, 6H of Thiopyrimidine), 10.5 (s, 1H,-OH) ppm M.S. (m/z) : 568 [M^+ ion], 566,501,500,499,498.

Compound (11d).

IR (KBr): 3916, 3777,3335,1634, 1573, 1440,757,688. ^{1}H NMR (DMSO-d_6): δ1.9 (s, 3H, CH_3), 5.0 (s, 1H,-NH), 5.2 (s, 1H,-NH), 7.0-7.9 (m, 8H, Ar-H+ 5H of Thiopyrimidine), 8.6 (s, 1H, 6H of Thiopyrimidine), 12.0 (s, 1H,-OH) ppm ^{13}C NMR (DMSO-d_6) : δ 48, 55, 113, 118, 122, 124, 126, 130, 135, 140, 150, 158,178,184. M.S. (m/z) : 465[M^+ ion], 433, 416, 408, 389.



Chalcone **Thiourea** **Thiopyrimidine (11a-h)**

R_1 = H,I,Br,Cl; R_2 = H, CH_3; R_3 = Cl,CH_3;

Table 1: Physico-chemical data synthesized Thiopyrimidine derivatives

Entry	Product	R_1	R_2	R_3
1	**11a**	H	H	Cl
2	**11b**	I	H	Cl
3	**11c**	Br	H	Cl
4	**11d**	Cl	H	Cl
5	**11e**	H	CH_3	Cl
6	**11f**	I	CH_3	Cl
7	**11g**	Br	CH_3	Cl
8	**11h**	H	H	CH_3

Entry	**Product**	**Mol. Formula**	**Yield %**	**M.P. °C**
1	11a	$C_{20}H_{16}ON_4Cl_2S$	88	132
2	11b	$C_{20}H_{15}ON_4Cl_2IS$	85	164
3	11c	$C_{20}H_{15}ON_4Cl_2BrS$	83	138
4	11d	$C_{19}H_{15}ON_4Cl_3S$	90	144
5	11e	$C_{21}H_{18}ON_4Cl_2S$	87	137
6	11f	$C_{21}H_{17}ON_4Cl_2SI$	83	155
7	11g	$C_{21}H_{17}ON_4Cl_2SBr$	90	199
8	11h	$C_{21}H_{19}ON_4ClS$	80	130

6. CONCLUSION:

In summary, we have designed and synthesized some new pyrazole containing thiopyrimidine derivatives was described The preliminary *in vitro* antimicrobial screening of this series revealed that, compounds showed potent activity. Therefore, the present study is useful drugs in medicinal investigation against bacterial and fungal diseases.

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A THEORETICAL STUDY OF THE REACTIONS OF •OH RADICAL WITH 8-OXOADENOSINE

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Abstract: *The oxidative damage to DNA bases commonly results in the formation of 7,8-dihydro-8-osoadenine (8-oxoA). The transient absorption spectrum for the reaction of the •OH radical with 8-oxoA has a peak at 325 nm which decayed with a rate of 1.5 x 10^4 s^{-1} to give another peak at 310 nm. The initial spectrum observed in the reaction of the •OH radical with 8-oxoA is assigned to the C4 and C5 OH adducts of 8-oxoA which then undergo dehydration to give the reducing neutral N-centred radical. The residual electron density of each atom of 8-oxoA was calculated using MoPro. The eleectron density supports the mechanism suggested where •OH radical forms an 8-oxoA at C5.*

Key Words: *Pulse radiolysis, 8-oxoA, hydroxyl radical, PM3 calculation*

1. INTRODUCTION:

The most important effect of radiation on the living cell is damage to the chromosome where the critical damage is that to the DNA component of the chromosome[1-3]. The study of the radiation chemistry of deoxyribose nucleic acid (DNA) leads to a better understanding of the chemical modifications induced in DNA by ionizing radiation. The major effects of ionizing radiation on cellular systems *e.g.* cell killing, radiation mutagenesis, radiation carcinogenesis and genome instability are caused either by direct absorption of the ionizing radiation by DNA (direct effect) or by the reaction of the DNA with radicals produced during the water radiolysis (indirect effect). The detailed knowledge of the reaction mechanism leading to the radiation induced DNA damage, identification of the type and quantity of damage will enable one to develop new models to study the radiation effects.

Radiation damage to DNA originates with the formation of free radicals [4,5] and includes structural damage due to the breakage of phosphate diester bonds leading to strand breaks, single as well as double, and changes in individual DNA bases. Both types of damage can be lethal or may lead to mutagenetic or carcinogenic changes. In human cell, the DNA is in a complicated polymeric form, the radiation chemical studies of DNA as such are difficult. Therefore, the relevant information on the mode of action of water radiolysis mostly comes from the study of isolated DNA and related model compounds.

The •OH radical has been shown to be the most important reacting species when the cell is exposed to ionizing radiations and it mainly reacts via addition to the pyrimidine and purine bases and by the minor process of hydrogen abstraction from sugar. The base moiety is the sole site of attack for the hydrated electron and the phosphate group largely remains inert towards these radicals.

The chemistry of the •OH radical induced oxidation of adenine includes the C8 •OH adduct can form 7,8-dihydroadenine (8-oxoA) or undergoes ring opening to give 2,6-diamino-5-formamido-4-hydroxypyrimidine (FAPy-A) depending on the reaction conditions.

The reaction of 7,8-dihydro-8-oxoadenine (8-oxoA), structure shown in Fig. 1 with the OH radicals is studied using semi empirical calculations and compared with the experimental observed results.

2. MATERIALS:

7,8-dihydro-8-oxoadenine (8-oxoA) (Berry & Associates Inc.) were of high purity and were. The other chemicals used in the study e.g. acetone, acetonitrile, potassium hydrogen phthalate, potassium persulphate, sodium azide, sodium hydroxide, perchloric acid, sodium carbonate, sodium bicarbonate, were from Qualigens (Mumbai) or Sigma and Aldrich. High purity grade N_2 (Industrial Oxygen Ltd.), N_2O (Indian Oxygen Ltd.) were used for degassing.

3. METHODL:

Semi empirical quantum calculations using PM3 [6] method were carried out to evaluate the possible sites of the •OH radical attack using the program MoPro [7]. The residual atomic charges from the MoPro analysis for the optimized structure of 8-oxoA are displayed in Table 3.1. Prior to the semi empirical calculations, the structure was optimized using MoPro. The optimized structure of 8-oxoA is shown in Fig. 2.

The pulse radiolysis experiments were carried out using a 4.3 MeV Mullard Linear Accelerator, SL46 with optical detection. The photomultiplier signals were stored using a Datalab transient digitizer (Model DL 905) interfaced with PC 386/20 which utilizes a customized version of ASYST Software (Technologies Inc.) to process the data. The details of the linear accelerator and the data handling are published earlier [8,9] Appropriate glass filters and shutter were used to minimize the effect of photolysis. The experimental results of the studies of radiation induced reactions with 8-oxoA have already been reported [10] and the aim of this study to compare the experimental results obtained with the theoretical studies.

4. RESULTS AND DISCUSSION:

The charge distribution for all the atoms of 8-oxoA are shown in Table 1. Adenosine is reported to react by addition mechanism to the C4 and C5. As is evident from the table, C5 has the highest residual of -0.298 but the electron density at C4 is almost negligible. Thus it can be supposed that the OH addition to 8-oxoA will take exclusively at the C5 position as the C5 more activated towards an electrophilic attack.

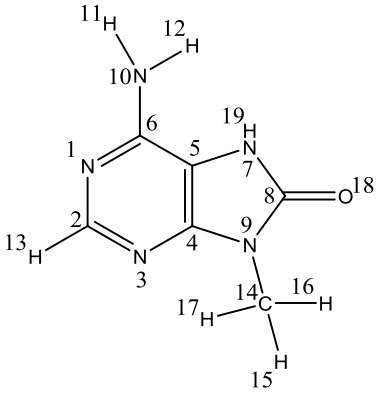


Fig. 1: The structure of 8-oxoA with the atoms numbered as a reference for theoretical calculations.

The electron rich C5 can be explained in terms of +I and +R effect of the neighbouring nitrogen atoms where the electron deficient C4 can be explained because the electron withdrawing nature of the adjacent groups. This result agrees with the experimental result where OH radical was found to react with 8-oxoA mainly by addition reaction.

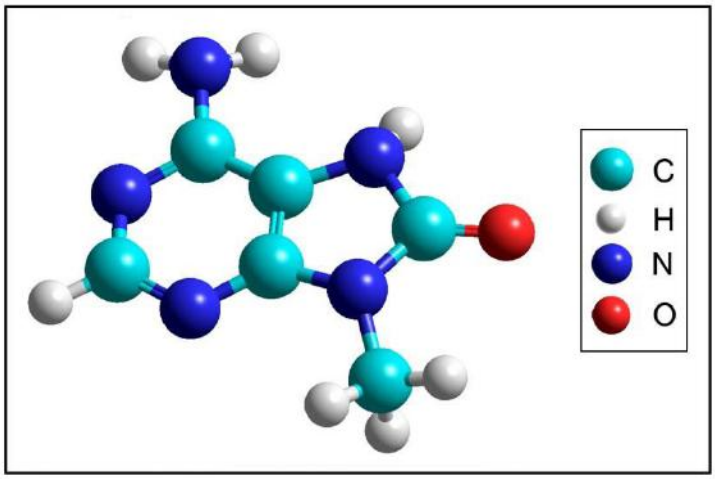
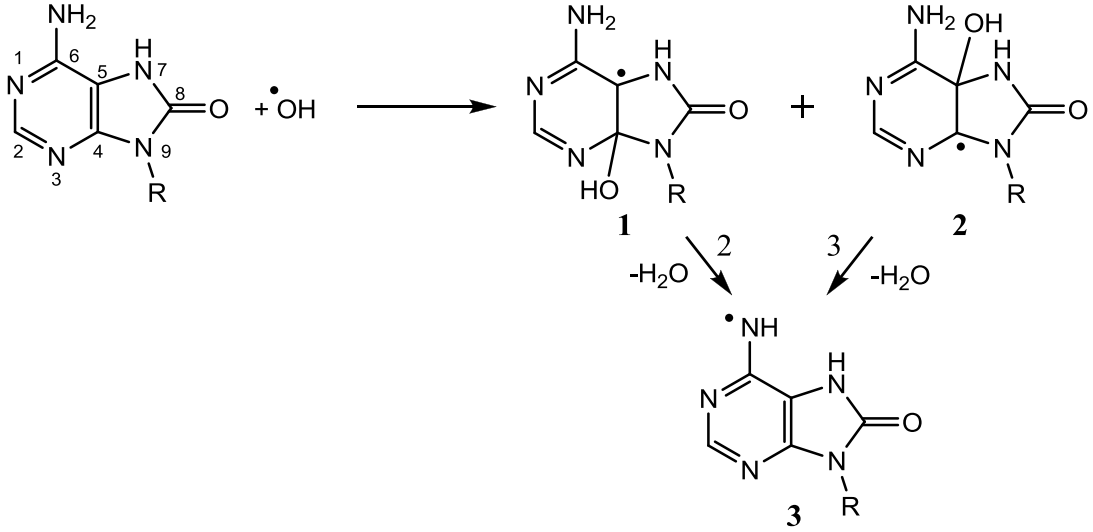


Fig. 2: The optimized structure of 8-oxoA using MoPro.

It is known that the $^{\bullet}$OH radical reacts by addition to C4, C5 and C8 positions of adenosine-the C5 adduct being a minor product and it is expected that the same reaction channel is also operative in 8-oxoA. Since, the $^{\bullet}$OH radical addition to the C8 position in these compounds is not possible and therefore, the formation of the C5 adduct assumes importance (it would be the major pathway) with the C4 adduct being a minor product. The initial absorption spectrum with maximum at 330 nm measured in the reaction of the $^{\bullet}$OH radical with 8-oxoA is attributed to the C4 and C5 adducts (reaction, Scheme 1). Both the $^{\bullet}$OH adducts (radicals **1** and **2**) subsequently undergo dehydration to form N6 centred radical **3**.

The heat of formation (ΔH_f) of a compound reflects its stability and the ease with which it is formed. The PM3 heats of formation of the isomeric $^{\bullet}$OH adducts at different positions of 8-oxoA for the equilibrium geometries. The ΔH_f values for the $^{\bullet}$OH adducts at C5 position are greater (10-12 kJ mol^{-1}) than the corresponding ones formed by the addition to the C4 carbon. The heats of formation of the $^{\bullet}$OH adducts of other carbons formed from the $^{\bullet}$OH attack

at NH_2 bonded carbon (~-35 kJ mol^{-1}) are larger than those estimated for other positions (~-60 kJ mol^{-1}) of 8-oxoA. Hence, the attack at carbon bonded to the amino group is less favourable in 8-oxoA.



Scheme 1: Mechanism for the reaction of the •OH radicals with 8-oxoA.

Table 1: The residual electron density at various atoms of 8-oxoA using PM3 method.

Sr. No.	Name of the Atom	Charge Density
1	N_1	-0.183
2	C_2	0.019
3	N_3	-0.139
4	C_4	-0.011
5	C_5	-0.298
6	C_6	0.018
7	N_7	0.117
8	C_8	-0.199
9	N_9	0.080
10	N_{10}	0.123
11	H_{11}	0.033
12	H_{12}	0.057
13	H_{13}	0.136
14	C_{14}	-0.067
15	H_{15}	0.069
16	H_{16}	0.071
17	H_{17}	0.042
18	O_{18}	-0.348
19	H_{19}	0.083

5. CONCLUSION:

The •OH radicals react with 8-oxoA at diffusion controlled rates with $k>10^9$ dm^3 mol^{-1} s^-. The transient absorption maxima at 310-320 nm and 350-380 nm which are assigned to the •OH adduct radicals respectively. The •OH radical reaction mechanism involves addition to the C5 as a major product with C4 adduct a minor product. The PM3 calculations support the mechanism suggested in the earlier study whereby addition reaction is the major reaction pathway.

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EFFECT OF SALT STRESS ON GARLIC

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Abstract: *A pot culture experiment was carried out to study the effect of salt stress on the nutrient value and plant growth parameters of garlic plant. The salt stress was given to 30 days garlic seedlings at the interval of 3 days. Three replicates of 150mM, 250mM,and 350mMNaCltreated plants were maintained separately. The following parameters: shoot length, root length, leaf number and chlorophyll content, amount of carbohydrate, reducing sugar, protein, proline, and level of enzyme activity were studied in these three sets. It was found that the morphological characters decreased with increase in the interval of salt stress. The biochemical parameter such as carbohydrate level increased with increasing salt stress interval which showed that the plant is in some kind of abiotic stress. The carbohydrate level in350mM NaCl,treated plant revealed that the plant is respiring fast thereby breaking down its stored food in order to cope with stress situation. Whereas increase in proline level showed that the plant is under abiotic stress. The activity of peroxidase was studied which showed makeable increase in the350mM NaCl, treated plant. This increase in the enzyme activity of the 350mM NaCl treated stressed plant showed that the plant is trying to struggle in order to acclimatize with the prevaling stress situation.*

Key Words: *Salinity stress, garlic(Allium sativum), in vivo study on the morphological parameters, biochemical parameters and enzyme activity.*

1. INTRODUCTION:

Soil salinity has become a global problem. A large number of lands are being eroded by salt. Soil salinity, one of the major abiotic stress affecting germination, crop growth and productivity is a common adverse environmental factor.High salinity causes both hyper ionic and hyper osmotic stresses and can lead to plant death (Hasegawa et al. 2000).According to the incapacity to grow on high salt medium, plants have been classified as glycophytes or halophytes. Sairam and Tyagi (2004) reported that most plants are glycophytes cannot tolerate salt stress.Parida and Das (2005) reported that during the onset and development of salt stress within a plant, all the major processes such as photosynthesis, protein synthesis and energy and lipid metabolisms are affected.In general biochemical, morphological and anatomical characteristics of crop species directly affected by soil salinity were well established (Ashraf, 2004; Ashraf and Harris, 2004;Chinnusamy et al., 2005; Parida and Das, 2005; Bhosale and Shinde, 2011a, b; Shinde etal., 2013; Shinde and ManjushaKhanna, 2014; Shinde and KetakiVaidya, 2014;Shinde and Jaya Thakur, 2015a, 2015b, 2016). There are many reports whichconcluded that salinity induces water deficitin many crops such as corn, sunflower, potatoand soybean (Katerji et al., 1996; Katerji et al., 2004). A primaryresponse in plants affected by salt stressshows decrease in plant water potential togreater extent, resulting in degradation inwater use efficiency, which leads to toxicdamages and overall reduction in yield (Glennand Brown, 1998; El-Hendawy et al., 2005). The earliest response is a reduction in the rate of leaf surface expansion followed by cessation of expansion as the stress intensifies but growth resumes when the stress is relieved.Yokoi et al., (2002) observed that plants are either dormant during the salt episode or there must be cellular adjustment and the response is species and genotypes dependent and depends on the length and severity of the salinity, the age and stage of development, the organ and the cell type and the sub-cellular compartment.Yamada et al.,(2003) observed that glycinebetaine (quaternary ammonium compound) and proline (amino acid) play an adaptive role in mediating osmotic adjustment and protecting the sub cellular structures in stressed plants. Mittova et al., (2002) demonstrated that higher salt tolerance of wild tomato (*Lycopersiconpennellii*) as compared to cultivated tomato (*Lycopersiconesculentum*) could be correlated with increased activities of SOD (superoxide dismutase), APX (ascorbate peroxidase), and POD (guiacol peroxidase).Ashraf and Harris (2004) reported that the agronomic parameters used for salt tolerance are yield, survival, plant height, leaf area, leaf injury, relative growth.

2. MATERIALSAND METHODS:

In this experiment, the garlic bulb was broken into individual cloves and 5 cloves were sown in four polythene bags in the Botanical garden of Fergusson College, Pune. After one month, mature plants were treated with different concentration of NaCl solution and effect of salinity stress was studied in vivo.

The replicates were treated with different concentration ofNaCl solution of 150mM, 250mM and 350mM respectively and the replicate in which salt stress was not given was kept as control. Plants were irrigated with this

solution for two days continuously. On the third days, plants were collected and the data was recorded that included root length, shoot length, leaf number, and different types of biochemical parameters.

2.1 MORHOLOGICAL PARAMETERS:

The plants were uprooted after the treatment of 48 hours.All plants in the experiment were not uprooted at a time only 5 plants were uprooted so as to record the result in an average.The root and the shoot length were measured in cm using the graph paper. The leaf number was also calculated so that the health of the plant can be assessed. The growth vigor index was calculated by using the data of root and shoot length. (Table 1)

2.3 BIOCHEMICAL PARAMETERS:

Estimation of Chlorophyll: Chlorophyll a, chlorophyll b,and total chlorophyll of garlic leaves were estimated using Arnon's (1949) method. The absorbance was read at 643, 652 and 663 nm using spectrophotometer. (Table 2)
Estimation of Carbohydrate: The soluble carbohydrate in garlic was estimated by Anthrone reagent as per the method given by Hansen and Moller (1975). The absorbance was read at 630 nm. (Table 3)

Estimation of Reducing Sugar: The reducing sugar of garlic was extracted by Dinitrosalicyclic acid method, Miller's(1972) method. The absorbance was recorded at 540nm. (Table 3)

Estimation of Protein: The protein was estimated by Lowry*et al.,* (1957) method. The absorbance was read at 660 nm. (Table 4)

Estimation of Proline: The proline content of garlic was determined by Bates*etal.*,(1973) method. The absorbance was read at 520 nm (Table 4).

Estimation of Peroxidase: The amount of peroxidase in garlic was determined by Malik (1980) and Putter (1974) method. The absorbance was read at 436 nm(Table 5).

3. RESULT:

Shoot length of the plant kept as control was found to be nearly 20 cm, i.e.18.5cm with more or less deviation of 1.5cm. The plant treated with salt concentration of 150mM, was of 19cm with a deviation of 1.23cm. As the concentration increases to 250mM, the shoot length was decreased to 17cm with more or less deviation of 0.56cm and further again with the increase of concentration the shoot length decreased significantly. (Table1). Root length of control plant measured about 5.9cm with a deviation of 0.9cm. As the concentration increases to 150mM there was reduction of root length by 1cmand for 250mM concentration it was seen to be further reduced to 3cm with a deviation of 1cm. (Table 1)

The leaf number of control plant was counted to be 5 per plant, with a deviation of 0.5. As the concentration increases to 150mM there was reduction of leaf number, and for 250mM concentration it was seen to be further reduced to 3 per plant. (Table 1)

3.1 Effect On Photosynthetic Pigments

Chlorophyll is the one of the major component of photosynthesis, when we induce the salt stress, the amount of chlorophyll 'a' count of the control plant was found to be 0.44mg/g and chlorophyll 'b' was 0.31mg/g, for 150mM concentration the chlorophyll 'a' count was 0.43mg/g and chlorophyll 'b' was 0.30mg/g and for 350mM the chlorophyll count was found lesser, i.e. amount of chlorophyll 'a' was 0.34mg/g and chlorophyll 'b' was 0.24mg/g.(Table 2)

3.2 Effect on the amount of reducing sugar, carbohydrates, protein and proline.

The reducing sugar parameter of control plant was found to be 1.50mg/g, the plant with 150mM concentration of salt stress showed little less reducing sugar level than the control plant and it was found least in 350mM stressed plant, i.e. 0.90mg/g. (Table 3)
Carbohydrate level of control plant was 1.40mg/g whereas the plant with 150mM salt concentration was measured as1.32mg/g. However the plant with 250mM was recorded to be 1.46mg/g and further increased was observed in 350mM. (Table 3)
Protein: The protein amount in control plant was measured about 21.46mg/g, it decreased in 150mM salt concentration i.e. 20.56mg/g and the plant with 250mM was about 18.00mg/g. However it was increased in 350mM salt concentration which was about 17.78mg/g. (Table 4)
Proline: The proline content in control plant was about 0.13mg/g, it increased in 150mM, 250mM, and 350mM, respectively and was about 0.19mg/g,0.23mg/g and 0.27mg/g. It was seen that as salt concentration increased proline level was also increased significantly. (Table 4)

3.3 Effect Of Enzyme Activity

Peroxidase: The enzyme showed considerable increase with increasing salt concentration, which exhibits the stress condition faced by the plant. (Table 5)

Table1 Effect of salt stress on morphology of garlic. Graph 1, 1.1and1.2

Treatment	Shoot Length(cm)	Root Length(cm)	Leaf number	GVI
Control	20±1.50	5±0.9	6±1	2500
150Mm	19±1.23	4±0.3	4±1	2300
250mM	17±0.56	4±0.1	4±1	2100
350mM	15±0.85	3.0	3±1	1800

ANOVA was carried out and it was significant at 5% level of probability.

Tabel-2 Effect of salt stress on chlorophyll pigment. Graph 2

Treatment	Amount of chlorophyll 'a'(mg/g)	Amount of chlorophyll 'b'(mg/g)	Total chlorophyll(mg/g)
Control	0.44	0.31	0.75
150mM	0.43	0.30	0.73
250mM	0.41	0.28	0.69
350mM	0.34	0.24	0.58

ANOVA was carried out and it was significant at 5% level of probability.

Table 3Effect of salt stress on Carbohydrate and Reducing sugar Graph 3

Treatment	Amount of reducing sugar(mg/g)	Amount of carbohydrate(mg/g)
Control	1.50	1.40
150 mM	1.45	1.32
250 mM	1.20	1.46
350 mM	0.90	1.73

ANOVA was carried out and it was significant at 5% level of probability.

Table 4 Effect of salt stress on Protein and Proline Graph 4.1, 4.2

Treatment	Amount of protein(mg/g)	Amount of proline(mg/g)
Control	21.46	0.13
150mM	20.56	0.19
250mM	18.00	0.23
350mM	17.78	0.27

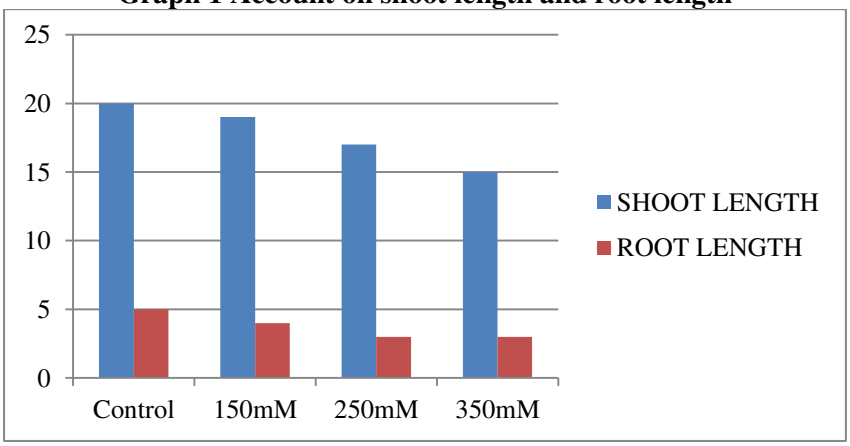
ANOVA was carried out and it was significant at 5% level of probability.

Table 5 Effect of enzyme activity peroxidase Graph 5.

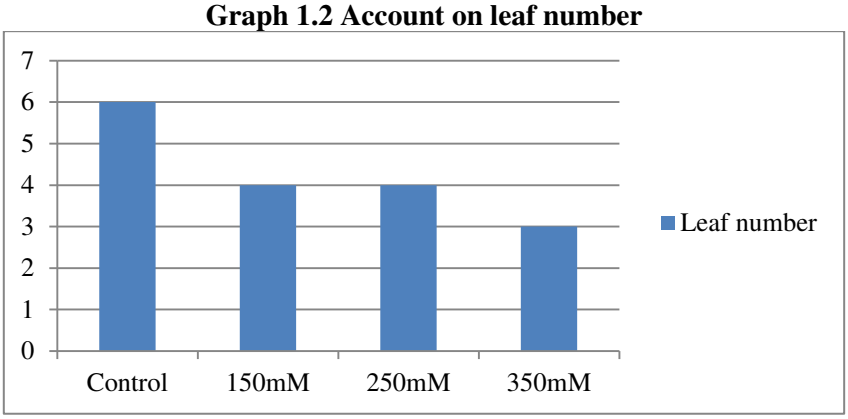
Treatment	Timerecorded for the enzyme	Enzyme activity (unit/L)
Control	60sec	4.12
150mM	55sec	6.09
250mM	40sec	7.21
350mM	25sec	13.21

ANOVA was carried out and it was significant at 5% level of probability

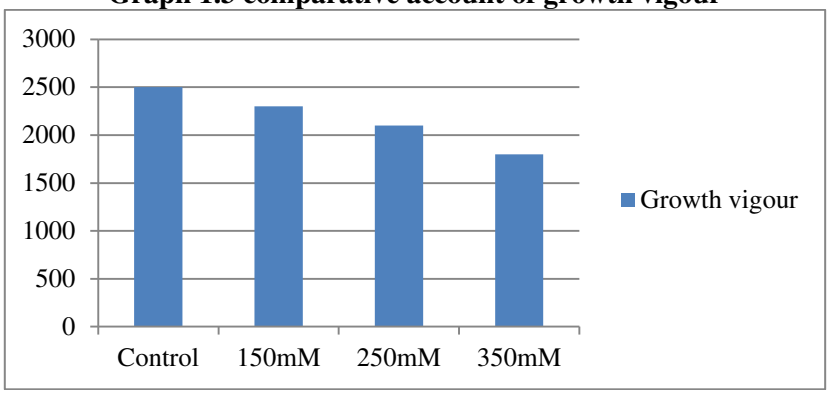
Graph 1 Account on shoot length and root length



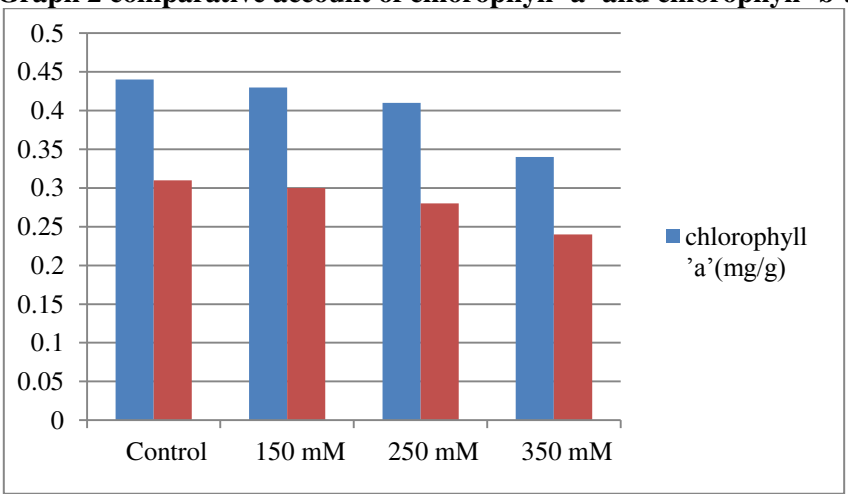
Graph 1.2 Account on leaf number



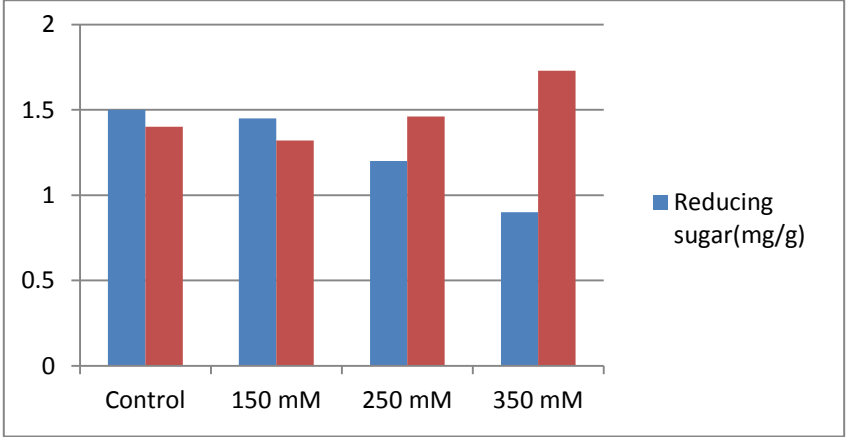
Graph 1.3 comparative account of growth vigour



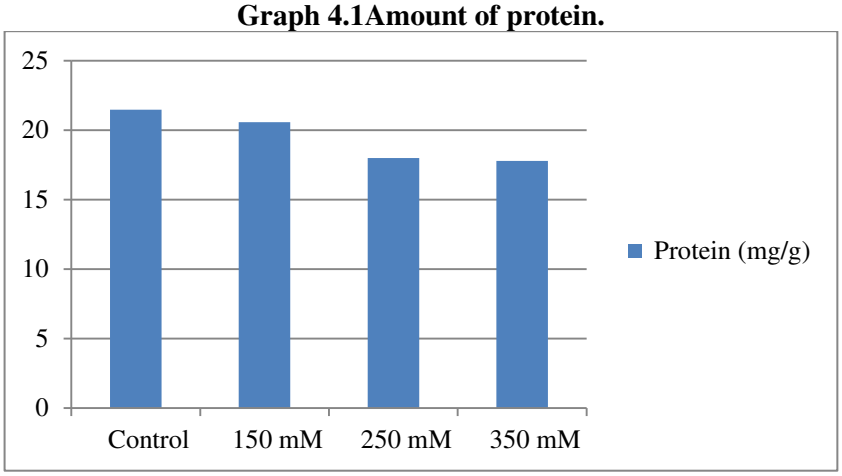
Graph 2 comparative account of chlorophyll 'a' and chlorophyll 'b'.



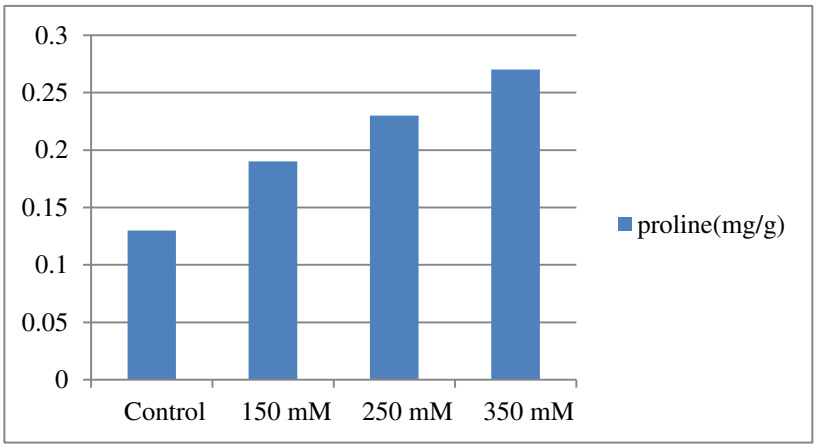
Graph 3, comparative account of Reducing sugar and Carbohydrates.



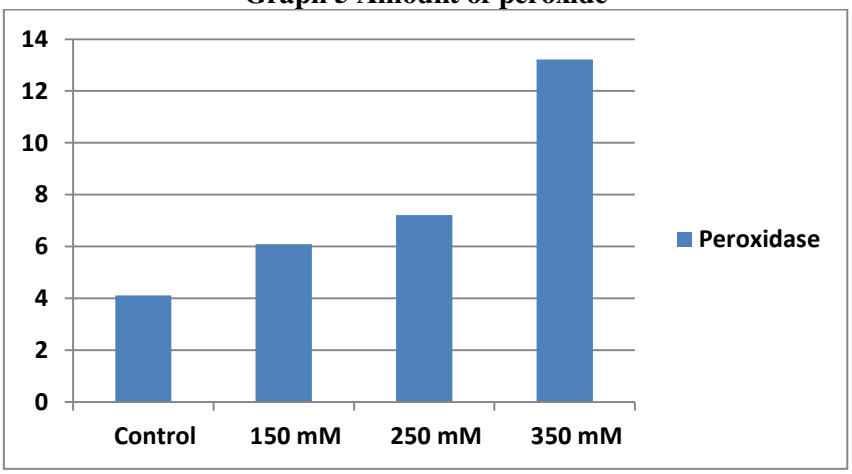
Graph 4.1Amount of protein.



Graph 4.2 Amount of proline



Graph 5 Amount of peroxide



4. DISCUSSION:

Khodarahmpour et al. (2012) observed drastic reduction in germination rate (32%), length of radicle (80%) and plumule (78%), seedling length (78%) and seed vigor (95%) in *Zea mays* seeds exposed to 240 mMNaCl. These coincide with the findings as the root length, shoot length and the leaf number decreased with high concentration of NaCl.The potential of salinity to inhibit root extension is shown by evidence that salinity can directly reduce cell wall extensibility.As photosynthetic electron transport is relatively insensitive to salts, either carbon metabolism or photophosphorylation may be affected due to salt stress (Sudhir and Murthy 2004) A positive correlation between salt stress induced photosynthetic rate and yield has been obtained in different crops (Pettigrew and Meredith 1994) .Same aspect have been observed in Garlic also as the carbohydrate metabolism increased resulting in decrease in the rate of photosynthesis.Fisarakis et al. (2001) reported a positive growth inhibition caused by salinity associated with a marked inhibition of photosynthesis. Hoque et al. (2008) showed that Proline protein improves salt tolerance in *Nicotianatabacum* plants by increasing the activity of enzymes involved in the antioxidant defense system.Proline

profile of slat stressed garlic specimen also showed marked increase which helped the plant to face the physiological water stress condition. AzevedoNeto et al. (2005) reported that addition of H_2O_2 to the nutrient solution induces salt tolerance by enhanced activities of antioxidants and reduced peroxidation of membrane lipids in leaves and roots of maize as an acclimation response. The same response was seen in case of peroxidase enzyme which showed high activity with 350mM salt concentration.

5. CONCLUSIONS:

Following information showed that the treatment of sodium chloride reduced the studied parameters like shoot length, root length, leaf number, chlorophyll content, reducing sugar, protein whereas parameters likes total carbohydrate, proline, peroxidase showed marked increase. The parameter which showed makeable increase with the increase in salt stress condition revels that the plant is trying to cope with the change natural state by increase in carbohydrate content, prolineand the enzyme activity of peroxidase.

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EVALUATION OF EFFECT OF DROUGHT STRESS ON *ALLIUM CEPA*

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Abstract: *A pot culture experiment was carried out to study the effect of drought stress on the nutrient value and plant growth parameters of onion plant. The drought stress was given to 30 days onion seedlings at the interval of 2, 4 and 6 days .Three replicates of each drought stress interval were maintained separately. The following parameters: shoot length, root length, leaf number, growth vigor index, amount of proline and the level of enzyme activity were studied in these three sets. It was found that the morphological characters decreased with increase in the interval of drought stress. The biochemical parameters such as proline and peroxidase showed makeable increase in the 6 day's stressed plant. The increase in proline level indicates that the plant is under abiotic stress. Moreover the increased enzyme activity of the 6 day's stressed plant showed that the plant is trying to struggle in order to cope with stress situation.*

Key Words: *Drought stress, onion (Allium cepa), in vivo study on the morphological parameters, biochemical parameters.*

1. INTRODUCTION:

Agricultural water deficit arises from both insufficient rainfall and soil water during the growing season to sustain a high crop yield [1].Plants are frequently exposed to drought and heat stresses that reduce crop yield worldwide. It is one of the major causes of crop loss worldwide; reducing average yields for most major crop plants by more than 50% [2].Soil drought inhibits plant growth and development. The dry matter reduction in wheat under water deficiency stress [3].Variability for proline metabolism has been reported in various crop species, but it is not well known whether accumulation of this amino acid contributes to the susceptible or tolerant nature of the genotypes [4].Plant drought tolerance involves changes at whole-plant, tissue, physiological and molecular levels. The root characteristics such as biomass, length, density and depth are the main drought avoidance traits that contribute to final yield under terminal drought environments [5]. A deep and thick root system is helpful for extracting water from considerable depths [6]. At a morphological level, the shoots and roots are the most affected and both are the key components of plant adaptation to drought. Plants generally limit the number and area of leaves in response to drought stress, just to cut down the water at the cost of yield loss .Since roots are the only source to acquire water from soil, root growth, its density and size are key responses of plants to drought stress .The antioxidant defense system in the plant cell constitutes both enzymatic and non-enzymatic components. The reactive oxygen species in plants are removed by a variety of antioxidant enzymes and water soluble scavenging molecules[7]. The antioxidant enzymes being the most efficient mechanisms against oxidative stress [8].

2. MATERIALS AND METHOD:

In this experiment, the onion bulbs were sown in four polythene bags. After one month, mature plants were subjected to drought stress and the effect of drought stress was studied in vivo. Three replicates of each set were maintained and were give drought stress at the interval of 2, 4 and 6 days. Plants in which watering was done regularly were kept as control. Plants which were irrigated after 2, 4 and 6 days interval were considered as drought stressed plants. After the end of every watering period as mentioned above, the plants leaves was collected and the data was recorded that included morphological and biochemical parameters. The data was recorded for three trials each.

3. MORHOLOGICAL PARAMETERS:

The plants were uprooted after the treatment of 48 hours. All plants in the experiment were not uprooted at a time only 5 plants were uprooted, so as to record the result in an average. The root and the shoot length were measured in cm using the graph paper. The leaf number was also calculated so that the health of the plant can be assessed. The growth vigor index was calculated by using the data of root and shoot length.

4. BIOCHEMICAL PARAMETERS:

Estimation of Proline: The proline content of garlic was determined by Bates et al., method. The absorbance was read at 520 nm.

Estimation of Peroxidase: The amount of peroxidase in garlic was determined by Malik and Putter method. The absorbance was read at 436 nm.

5. RESULT:

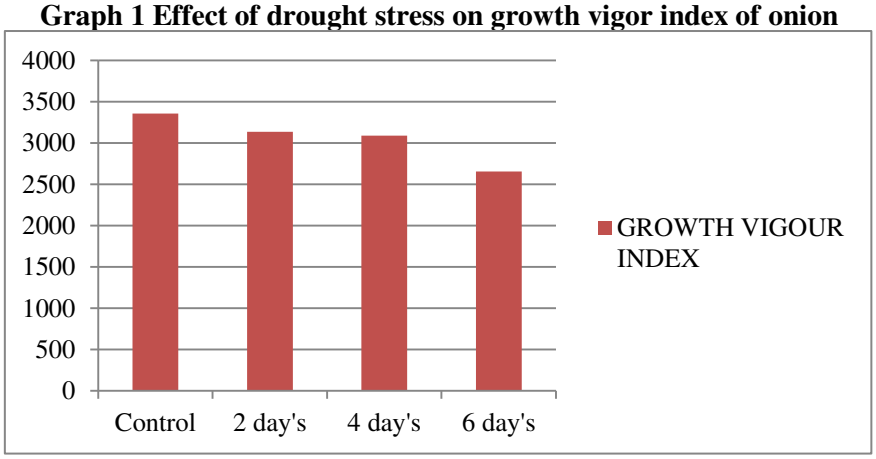
Shoot length of the plant that is kept as control was found to be nearly 28 cm, i.e.27cm with more or less deviation of 1.12 cm, respectively. In the replicates which were subjected to 2 days of drought stress, the shoot length was recorded to be 26 cm with a deviation of 1.89 cm. As the period of drought stress increased consequently the shoot length decreased proportionally. Root length of control plant measured about 6.54 cm with a deviation of 1.25 cm. On the other hand the last replicate of plants which were subjected to 6 days of drought stress showed marked difference in root length which was found out to be 3.55 cm with a deviation of 2.66 cm respectively. Leaf number was recorded significant less in the last replicate's which was subjected to 6 days of drought stress followed by the replicate of 4 days set of plants. It was observed that the number of leaf in the control set of plants were 8±2. But in the last replicate of plant which were devoid of water for consequent 6 day had 4±1 number of leaf respectively. The proline amount in control plant is measured about 0.12 mg/g, the amount of proline showed marked increase with the increase of stress. As in the replicates which were given water stress in an interval of 2 days the proline content was measured to be 0.20 mg/g, followed by 4 days drought stress replicates which also showed increase in the proline content i.e., 0.23 mg/g. Lastly, in the last set of replicates which were given prolong drought stress for 6 days continuously the proline content increased significantly which was recorded to be 0.28 mg/g. The enzyme activity of peroxidase in the control plant and the replicate which received drought stress in an interval of 2 days is considerably negligible, but the enzyme activity was well pronounced in those replicate which was subject to drought stress for 4 days as well as for the 6.

Table 1 Effect of drought stress on morphology of onion

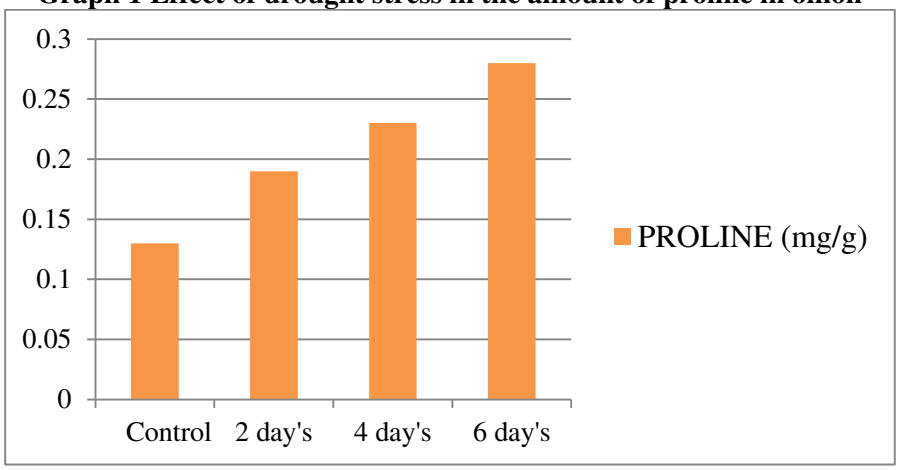
Treatment	Shoot Length (cm)	Root Length (cm)	Leaf number	GVI
Control	27±1.05	6.54±1.25	8±2	3354
2 day's	26±1.89	5.33±0.91	6±1	3133
4 day's	26±0.23	4.88±1.05	6±1	3088
6 day's	23±1.27	3.55±2.66	4±1	2655

ANOVA was carried out and it was found significant at 5% probability level

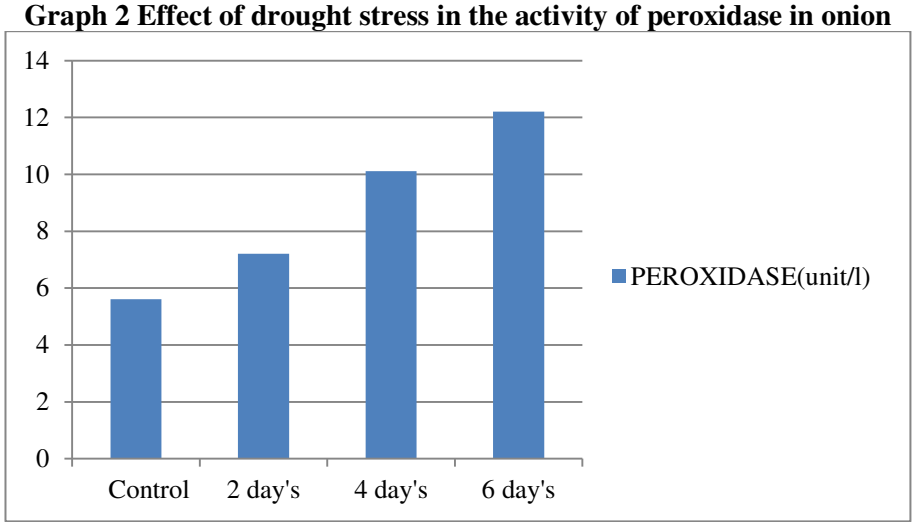
Graph 1 Effect of drought stress on growth vigor index of onion



Graph 1 Effect of drought stress in the amount of proline in onion



Graph 2 Effect of drought stress in the activity of peroxidase in onion



6. DISCUSSION:

Drought affects plant–water relations, reduces water contents of leaf and plant, causes osmotic stress and inhibits cell expansion and cell division as well as growth of plants as a whole [9]. In present study, drought stress reduced shoot length and leaf no.Roots are the key plant organ for adaptation to drought. If tolerance is defined as the ability to maintain leaf area and growth under prolonged vegetative stage stress, the main basis of variation appears to be constitutive root system architecture that allows the maintenance of more favorable plant water status [10]. The possession of a deep and thick root system allowed access to water deep in the soil, which was considered important in determining drought resistance in upland rice. Thus, the finding correlates with our result of root length considerably as with the increase in drought stress the root length considerably increased**.** The growth vigor index of drought stress plantswas less as compared to the control plants. In rice, drought stress during the vegetative stage greatly reduced the plant growth and development [11] which is in accordance with our result.Drought stress has diversified adverse effects on plant physiological and metabolic processes [12]. Important roles of proline under abiotic stress conditions including drought stress are well recognized. Proline has vital roles in osmotic adjustment, stress signal transduction; it also acts as an antioxidant. Increase of proline level under physiological stresses including drought stress conditions were documented previously [13]. Similarly profound increases of proline levels were observed in our species which were subjected to drought stress. The increase in the activity of scavenging enzymes like peroxidase could be a sign either of the severe oxidative stress or an efficient stress response mechanism [14]. In our experiment the enzyme activity of peroxidase was seen to be increased significantly in those replicates which were subjected to prolong drought stress.

7. CONCLUSION:

The present study indicates that water is essential for the growth and development of plant. The replicates which were subject to prolong drought stress showed marked decrease not only on the morphological parameters but also on the biochemical parameters. Our result suggested an important role of proline and antioxidant enzyme whose level was increase in order to protect the plant from stress and render it resistant against drought condition. The morphological parameters which were decreased due to drought stress actually helped the plant to fight against the stress situation.

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A Quantitative Structure–Reactivity Assessment Of Iodination Of 2-Nitrophenol And 4-Nitrophenol Using Molecular Iodine In Aqueous Medium Via Green Route By Hydrodynamic Voltammetry

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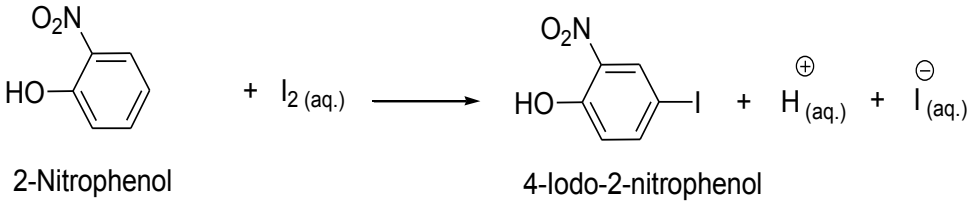
Abstract: *Iodination of aromatic substrates in aqueous medium are essentially electrophilic substitutions. Kinetics as an investigatory tool for the quantitative assessment of the structure–reactivity correlation in these reactions for a diverse range of substrates has rarely been reported, presumably due to the rapidity of these reactions in aqueous medium. Presently, hydrodynamic voltammetry has been adopted to investigate the rapid kinetics of uncatalyzed iodination of 2-Nitrophenol and 4-Nitrophenol at 7.0 pH and at 22. 5°C in aqueous medium. The velocity constants for 2-nitrophenol and 4-nitrophenol are found to be 52 $M^{-1}s^{-1}$ and 16700 $M^{-1}s^{-1}$ respectively, thereby quantitatively assessing the relative reactivity of these substrates. Both reactions follow green Chemistry principles. Iodo derivatives of aromatic substrates are precursors of many medicinally important drugs.*

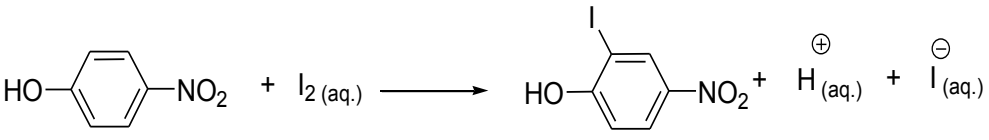
Keywords: *Molecular Iodine, Nitrophenol Regioisomers, Hydrodynamic Voltammetry.*

1. INTRODUCTION:

Halogenations of aromatic substrates in aqueous solution yield products that are often precursors of drug molecules. These are of pharmacological significance as anti-tumor, anti-viral, and anti-bacterial biomolecules[1]. They are of importance in organic synthesis in coupling reactions as well[2]. The reactivity of these substrates results of a host of cumulative factors like their nature, moieties present on them, substituent regiospecificity, steric compulsions of the reaction dynamics, reagent pH, and solvent. Though the reactivity of the substrates in these reactions have been qualitatively predicted, a quantitative assessment has been found lacking due to the immense rapidity of these reactions in aqueous medium. Special fast reaction techniques are needed for their study. Herein we have adopted the hydrodynamic voltammetry[3] technique to quantitatively measure the reactivity of 2- nitrophenol and 4-nitrophenol in aqueous medium .The substrates have been iodinated by molecular iodine in aqueous solutions devoid of iodide ions. The specific rates of iodination obtained, have been invoked to quantitatively justify the relative ease of the mechanistic route in these reactions and thereby estimate the reactivity of the regioisomers in this study.
The reactions studied presently are all rapid in aqueous medium and are as follows



2-Nitrophenol 4-Iodo-2-nitrophenol



4-Nitrophenol 2-Iodo-4-nitrophenol

2. MATERIALS:

Preparation of solutions:

Stock solutions of the supporting electrolyte potassium nitrate and the two regioisomers under study are prepared in conductivity water using AR grade chemicals. Aqueous iodine is prepared by dissolving iodine crystals in conductivity water devoid of iodide ions and standardized iodometrically.
Electrodes :The positive electrode is a platinum microcathode (RPE) rotating at 600 rpm. The negative electrode is the saturated calomel electrode (SCE)

3. METHOD:

Calibration of the diffusion current: Diffusion currents at the RPE for different concentrations of iodine solutions containing a hundred fold supporting electrolyte concentration are determined. The plot of diffusion current Vs concentration is found to be linear. A typical one is shown in Fig.1

4. DISCUSSION:

Kinetic readings: Equal concentrations of 4- nitrophenol and iodine are mixed in a thermostated reaction vessel containing the two electrodes and the time is noted. At every 5 seconds, the decreasing diffusion current values are recorded for about one half-life of the reaction. The experimental error in the readings is within 0.5 %.

5. ANALYSIS:

The plot of $[I_2]^{-1}$ Vs time is found to be linear. A typical one is shown in Fig.2.The slope of this plot is the specific reaction rate of the reaction under investigation. The procedure is repeated for 2-nitrophenol. Typical observations are presented in Tables 1-2.

6. FINDINGS:

$[I_2]$ / 10^{-5} M	Diffusion current / nA
0.2	6.1
0.4	11.1
0.6	16.0
0.8	21.0
1.0	25.0

Table 1 : Calibration of diffusion current for iodine at 22.5^{0}C in the iodination of 4-nitrophenol
Potential applied at the RPE versus SCE = 0.2 V

Time /s	Diffusion current / nA				$[I_2]$ / 10^{-5}M	$[I_2]^{-1}/10^4$M^{-1}
	1	2	3	Mean		
0	25.0	25.1	25.0	25.0	1.00	10.0
5	14.8	14.8	14.8	14.8	0.56	17. 9
10	10.0	10.0	10.1	10.0	0.37	27.0
15	7.6	7.6	7.6	7.6	0.28	35.7
20	7.1	7.0	7.0	7.0	0.23	43.5

Table 2 : Kinetics of iodination of 4- nitrophenol by molecular iodine at 22.5^{0}C Initial Concentration of iodine in the reaction mixture = 1 x 10^{-5} M

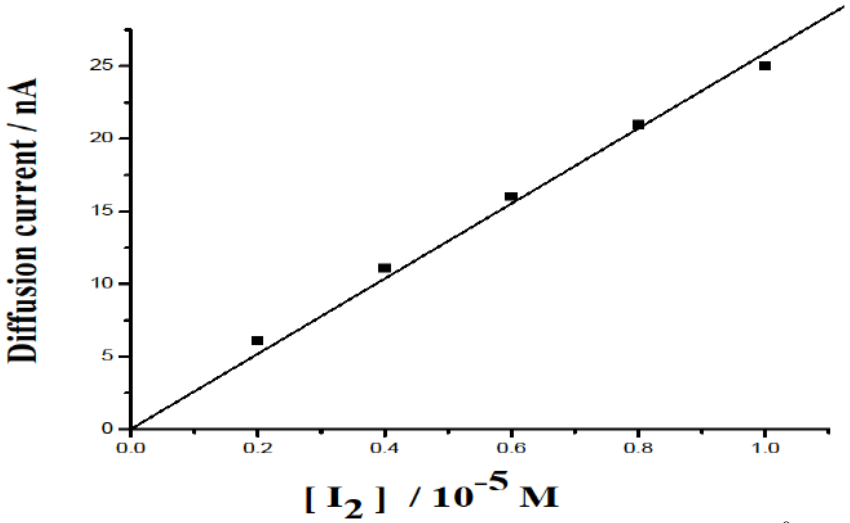


Figure1: Calibration of diffusion current of iodine at 22.5^{0}C

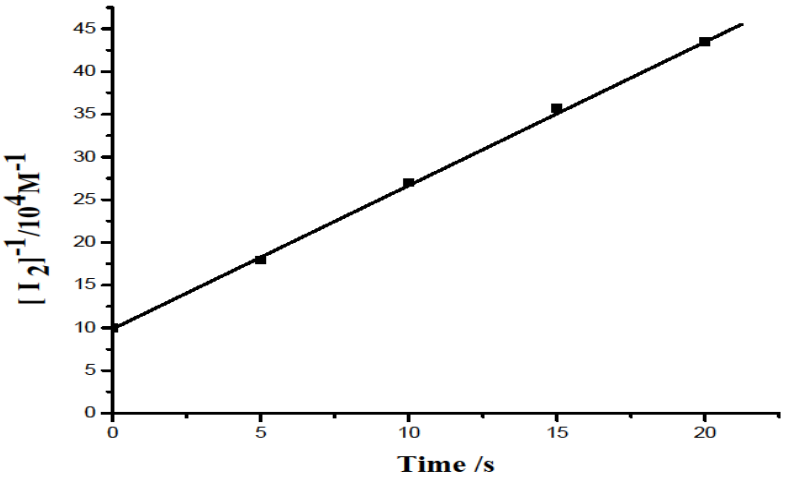


Figure 2: Kinetics of iodination of 4-nitrophenol by molecular iodine at 22.5^0C

7. RESULTS:

The iodination reactions of the two regioisomers are found to be rapid and follow second order kinetics as the plots of $[I_2]^{-1}$ Vs time are linear. The formation of the monoiodoo derivatives in both the cases is ascertained by stoichiometry and by NMR investigations. The velocity constants for 2- nitrophenol and 4-nitrophenol are found to be 52 $M^{-1}s^{-1}$ and 16700$M^{-1}s^{-1}$ respectively at 22.5^0C.

8. CONCLUSION:

4-nitrophenol shows a markedly high reactivity as evidenced by the specific reaction rate relative to 2-nitrophenol. The steric compulsion is reflected in the relative reactivity of the regioisomers under study in a quantitative manner.

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Synthesis And Srtuctural Studies On Polypyridine Coordination Compounds Of 2-(Aryl)Imidazo[F]1,10- Phenanthroline With Some Metal Ions

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Abstract: *Polypyridine complexes of the type $[M(N–N)_2(L)](OAc)_2$ where M is Cu(II), Co(II), Ni(II) and $(N-N)_2$ is 2,2'-bipyridine $(bpy)_2$ or 1,10-phenanthroline $(phen)_2$, (L) is 2-(aryl)imidazo[4,5-f][1,10]phenanthroline ligands, have been synthesized. The structures of the compounds were determined by elemental analysis, IR, UV-Vis., ^{1}H-NMR, ESR spectral studies, thermal studies and powder XRD. Elemental analysis data suggested that the complexes have a 1:2:1 molar ratio among the metal and ligands. The spectral data show that all the complexes were six coordinated and possess octahedral geometry around the metal ions. The powder XRD patterns of complexes recorded in the range (2θ = 0–80°) and average crystallite size (d_{XRD}) was calculated using Scherrer's formula. Thermal decomposition profiles of complexes show high decompound temperatures indicating a good thermal stability.*

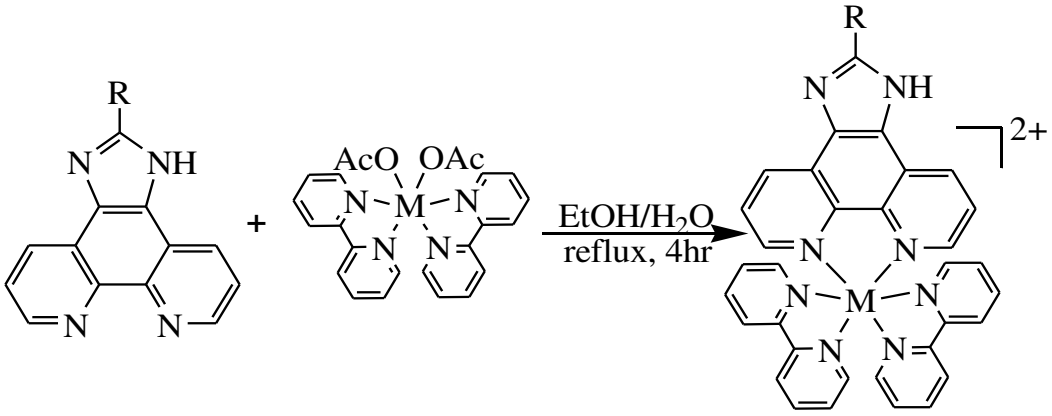
Key words: *1, 10-phenanthroline 5, 6-dione, arylimidazole and Polypyridine complexes.*

1. INTRODUCTION:

Polypyridyl complexes of transition metals with 1, 10-phenanthroline (phen) and its derivatives are very important ligands in organometallic chemistry because they have rigid framework and possesses a superb ability to chelate many metal ions via two nitrogen donors. Due to their high charge transfer mobility, bright light emission and good electro and photo active properties they provide potential for various technological applications. Complexes of these derivatives are of great interest since they exhibit numerous biological activities such as antitumor, anticandida, antimycobacterial, antimicrobial activitives. Furthermore, the interaction of these complexes with DNA has gained much attention due to their possible applications as new therapeutic agents.[1-3] This prompted us to synthesize some new metal complexes of phen imidazole derivatives. They were characterized using analytical and various spectral techniques.

2. MATERIALS:

1,10-phenanthroline 5,6-dione was obtained according to published procedure.[4] The compounds $[M(bpy)_2](OAc)_2.H_2O$ and $[M(phen)_2](OAc)_2.6H_2O$ were synthesized by a method similar to one described previously.[5] Other chemicals were purchased from Aldrich and used without further purification. The synthetic pathway for the compounds is shown in Scheme 1.



Scheme 1 Structure of complexes.

3. METHODS:

The complexes were synthesized by adding a calculated amount of the ligands in ethanol and water to the metal salt in the same solvent. The mixture was heated under reflux for 4 h, and then most of the ethanol was removed by evaporation. The solid complexes that separated out were filtered, washed with ethanol and dried under vacuum.

4. DISCUSSION:

ANALYSIS

Elemental Analysis

Elemental analysis data suggested that the complexes have a 1:2:1 molar ratio between the metal and ligands. i.e. one mole of metal acetate reacted with two moles of 1,10-phenanthroline or 2,2-bipyridine and one mole of ligands (L^1) or (L^2) or (L^3) to give the corresponding complexes. All the complexes show the analytical results close to the theoretical values indicating the presence of two types of ligands.

4. FINDINGS:

IR Spectra

The IR spectra of complexes are shown in Fig. 2. In the IR spectra of all complexes, the bands observed at 3055 cm^{-1} is due to stretching vibrations of the NH of the imidazole ring.The broadened band between 3421–3390 cm^{-1} is due to stretching vibration of phenolic OH. The same bands were observed in the IR spectra of ligands. This observation confirmed that phenolic OH and NH of the imidazole ring of ligands do not participate in coordination. The bands observed at 1623 cm^{-1} is due to the stretching vibration of the C=N of the imidazole ring were not significantly affected in their complexes indicating that nitrogen atom of this group is not involved in coordination for all complexes. On the other hand, the bands of the C=N (phenanthroline ring) and C=C (aromatic) groups were shifted to lower frequencies in all the complexes at 1558–1515 cm^{-1} and 1423–1361 cm^{-1} that indicates the participation of the C=N (phenanthroline ring) groups in coordination of the metal ion. The bands of the N–H and O–H–N groups in all the complexes shifted to negative frequencies after complexations. The negative frequency shifts of these groups may be attributed to flow of electrons from these groups to the phenanthroline ring due to electron flow from nitrogen atom of the phenanthroline ring to the metal ion after complexations.[6-8] New additional bands are observed at 3400 cm^{-1} as broad bands are due to OH stretching vibrations of H_2O molecules and at 640 cm^{-1} are due to M–N stretching vibrations.

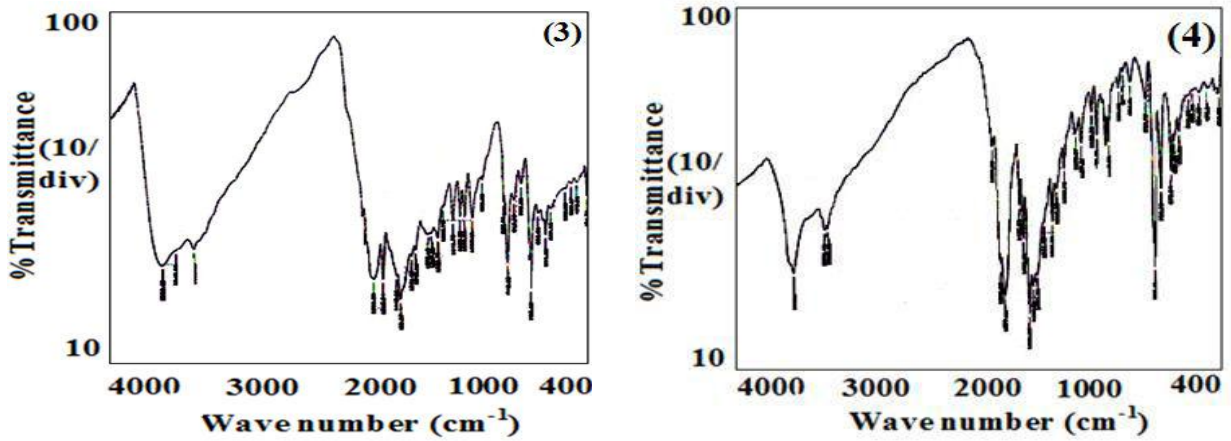


Figure 2 The IR spectra of ligand and complex.

Electronic Spectra

The electronic spectra of the complexes were recorded in DMSO as a solvent. In the electronic spectra of complexes the bands are observed at 262, 270 and 271 nm are originated from π–π* transitions of phenanthroline ring and the bands are observed at 285 nm in the spectra of complexes, are due to π–π* transitions of bipyridine ring. The bands observed at 345 nm in all the complexes were attributed to transitions of imidazole ring of ligands.[17-18] The electronic spectra of complexes exhibited three well defined bands in the range of 262–346, 270–428 and 271–345 nm, respectively. These bands were assigned to $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ transitions which corresponds to octahedral geometry.[8-10] The other weak absorption bands in the spectra of the complexes were contribution from spin allowed metal to ligand charge transfer, MLCT.

Powder XRD

Powder XRD patterns of complexes show the sharp crystalline peaks indicating their crystalline phase. The diffraction pattern of complexes (4) and (5) is measured in the range (2θ = 0–80°) are shown in Fig. 3. The crystallite size of the complexes d_{XRD} is estimated from XRD patterns by applying full width half maximum of the characteristic peak to Scherrer's equation using the XRD line broadening method. [11,12]

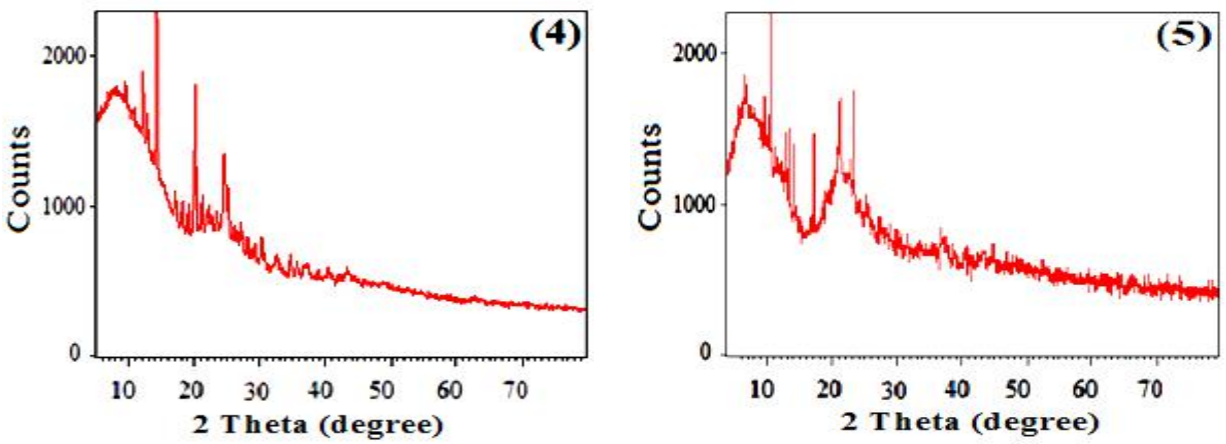


Figure 3. Powder XRD patterns of complexes.

Thermogravimetric study

Thermogravimetric studies have been made in the temperature range 25–1000 °C. The thermal stability data of the complexes are listed in Table 1. Thermal decomposition curves of the complexes showed a similar sequence of three decomposition steps [13] given in Fig. 4. The horizontal thermal curves observed above 710°C correspond to a metal oxide residue.

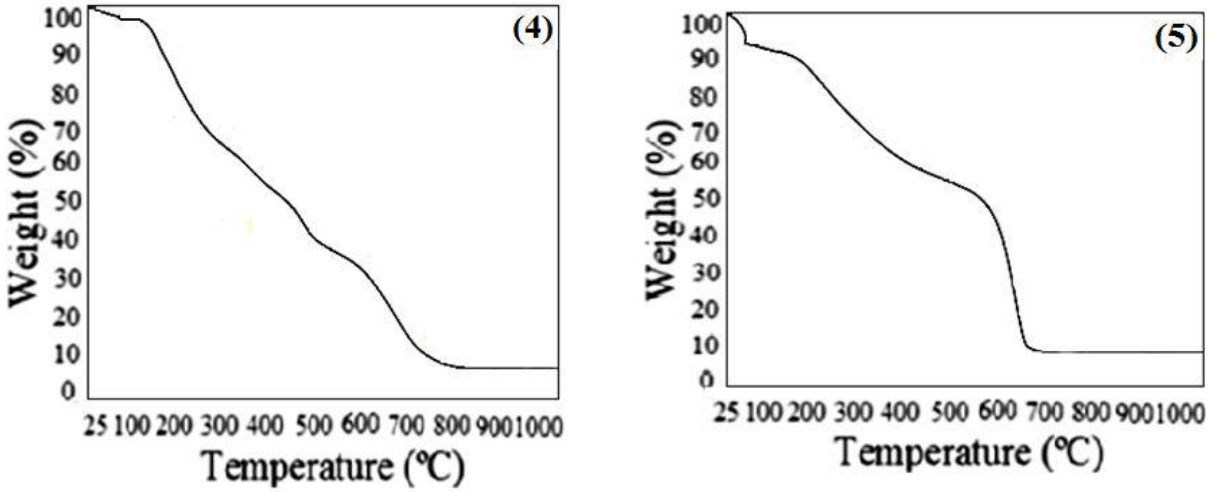


Figure 4 The TGA curve of the complexes.

5. CONCLUSION:

Polypyridine complexes of imidazole derivatives ligands were synthesized and characterized. Based on the above observations of the elemental analysis, UV-Vis., IR, ^{1}H-NMR, ESR spectral data it is possible to determine the type of coordination of the ligands in their complexes. The spectral data reveal that all the complexes were six coordinated and possess octahedral geometry around the metal ion. Powder XRD indicates the crystalline state of the complexes. Thermal property measurements show that the complexes have good thermal stability.

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EFFICIENT SYNTHESIS OF 2,4,5-TRIARYL IMIDAZOLE: AN ANTI-INFLAMMATORY

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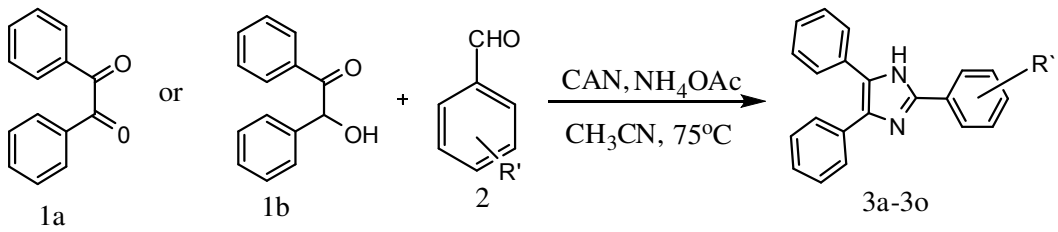
Abstract: An efficient and rapid one-pot synthesis of 2, 4, 5-triaryl imidazole is carried out at 75°C using aromatic aldehyde, benzil or benzoin in the presence of catalytic amount of ceric ammonium nitrate. Excellent yield in short reaction time is characterized by simple work up procedure and efficient recovery.

Key Words: ceric ammonium nitrate CAN, 2, 4, 5-triaryl imidazole, aromatic aldehyde , benzil, benzoin

1. INTRODUCTION:

The imidazole ring system is of particular interest as it is a component of histidine that produce histamine in metabolic process [1]. The potency and wide applicability of the imidazole pharmacophore can be attributed to its hydrogen bond donor-acceptor capability as well as its high affinity for metals which are present in many protein active sites.Triaryl imidazoles are used as a photosensitive materials in photography [2] .In addition they are of interest because of their herbicidal, analgesic [3], fungicidal [4], anti-inflammatory [5] and antithrombotic activities [6]. Recent advances in green chemistry and organo metallic chemistry have extended the boundary of imidazole to the synthesis and application of a large class of imidazoles as ionic liquids [23] and imidazole related N-heterocyclic Carbenes (NHC) [7] imidazoles also have COX-2 inhibitory activity [8]**.** Generally triaryl imidazoles are prepared by hetro-cope rearrangement [9] or by reaction of glyoxal, formaldehyde and ammonia [10-11]. Previous studies suggested the use of Zn-Al_2O_3 [12], and PCl_5[13] diktones aldehyde and ammonium acetate in phosphoric acid [14] as well as in H_2SO_4[15] and DMSO[16]. Micro wave assisted synthesis of imidazoles from 1,2-diketones in the presence of catalyst such as silica-gel[17],silica-gel/HY[18], MW/Al_2O_3[19], DMF[20] and MW/acetic acid[21].



Scheme-1

Reported methods have one or the other limitations such as harsh reaction conditions, poor yields prolonged time period, use of hazardous and expensive catalysts and polar solvents. Recently ceric ammonium nitrate (CAN) received considerable attention as an inexpensive, nontoxic, readily available catalyst for various transformations, affording the corresponding products in excellent yield with high selectivity, In the proposed work we have synthesized trisubstituted imidazoles from benzil or benzoin with aldehyde at 75°C in the presence catalytic amount of CAN (schem-1). During the course of our studies toward the development of new routs to the synthesis of biologically active heterocycles [22].

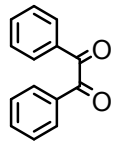
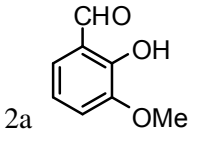
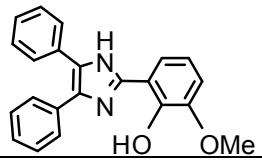
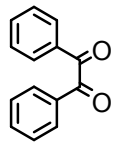
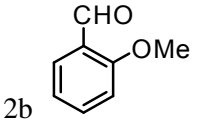
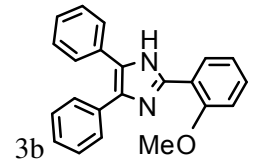
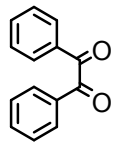
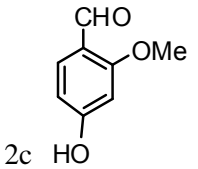
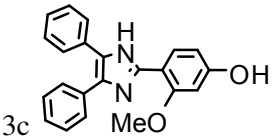
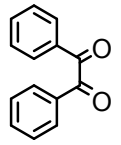
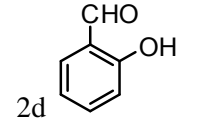
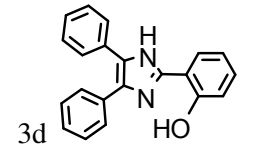
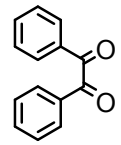
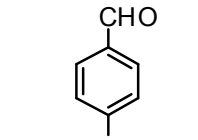
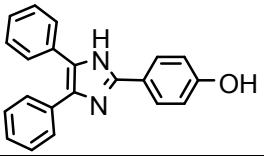
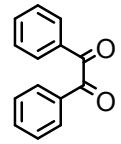
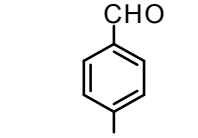
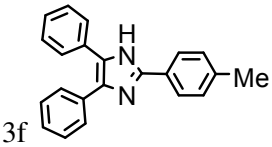
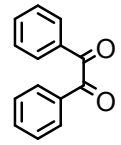
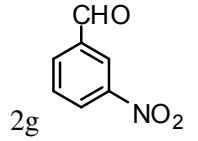
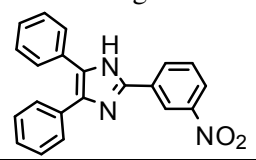
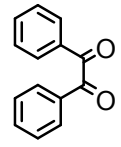
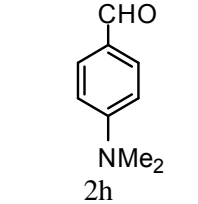
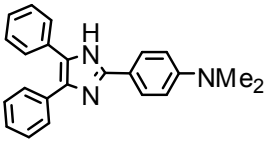
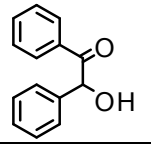
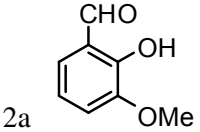
2. RESULT AND DISCUSSION:

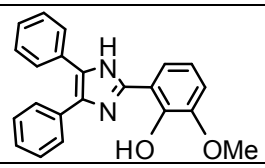
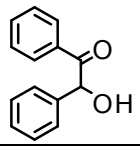
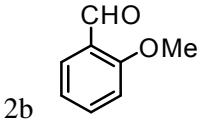
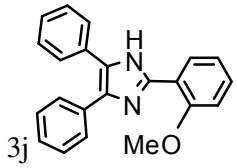
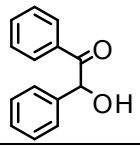
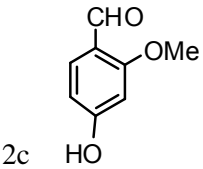
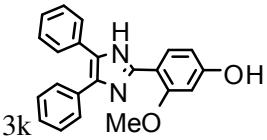
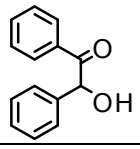
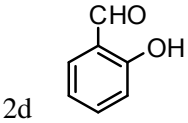
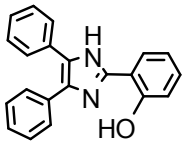
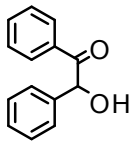
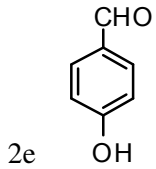
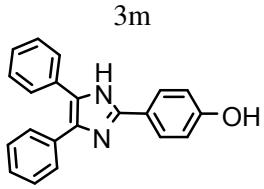
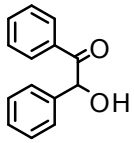
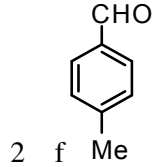
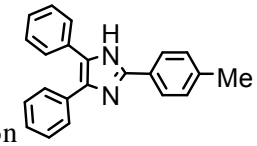
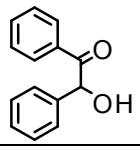
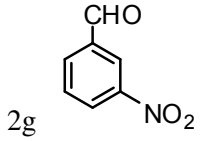
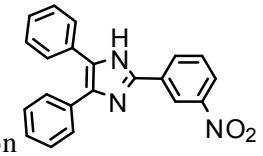
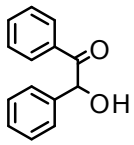
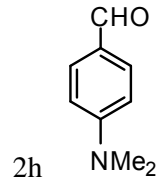
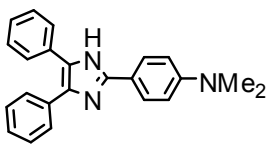
In continuation to our endeavous to develop the biologically active compounds of substituted imidazole derivatives, we have developed the methodology for the synthesis of 2,4,5 trisubstituted imidazoles using neat reaction condition . The synthesis of trisubstituted imidazole by aromatic aldehyde, benzil or benzoin and ammonium acetate in presence of ionic liquid [Hbim]BF4 is a well established procedure [23].However,ionic liquid is economically expensive not available easily. When benzil ,benzoin (1a,1b) and aromatic aldehyde 2 were treated with a catalytic amount of CAN in acetonitrile for 2-6 hrs, then triaryl substituted imidazole 3 were obtained in moderate to good yields (table 2).

To examine the catalytic activity of CAN, we explored a modification of the reaction of (1a) or (1b) and aromatic aldehyde in acetonitrile first without CAN then ,5mol%, 10mol%, 20mol%, 25mol% amount of CAN. The results are shown in table 1.According to observations in table 1 (10mol%) of CAN was enough and efficient ,as 90 %

.91% yield (entry 2) for both (1a) ,(1b) respectively an excessive amount of the catalyst was check for the same reaction condition it is found that at the same reaction time, % yield did not increase . (table 1 entry 3-5) .In the absence of CAN, no reaction was found (table1, entry 1) . To investigate the real catalyst species, CAN , CeSO4, the experiment using CeSO4 20mol% in place of CAN has been tried. The product was obtained in both 1a,1b with yield of 60%, 58% at 75°C (table 1 entry 6) hence CAN should be the real catalyst species because its Lewis acidity

Table:-1 Effect of catalytic amount of CAN[b]

Reactant 1a,1b	Reactant 2	Product 3	Time(h)	Yield(%)
	 2a	3a 	4	92%
	 2b	 3b	3.5	94%
	 2c	 3c	3	91%
	 2d	 3d	1.5	90%
	 2e	3e 	4	92%
	 2f	 3f	3.5	88%
	 2g	3g 	4.5	90%
	 2h	3h 	3.5	93%
	 2a	3i	4	89%

				
	 2b	 3j	4	90%
	 2c	 3k	3	92%
	 2d	 3l	4	90%
	 2e	3m 	3	92%
	 2 f	 3n	3	90%
	 2g	 3n	5	89%
	 2h	3o 	3.5	88%

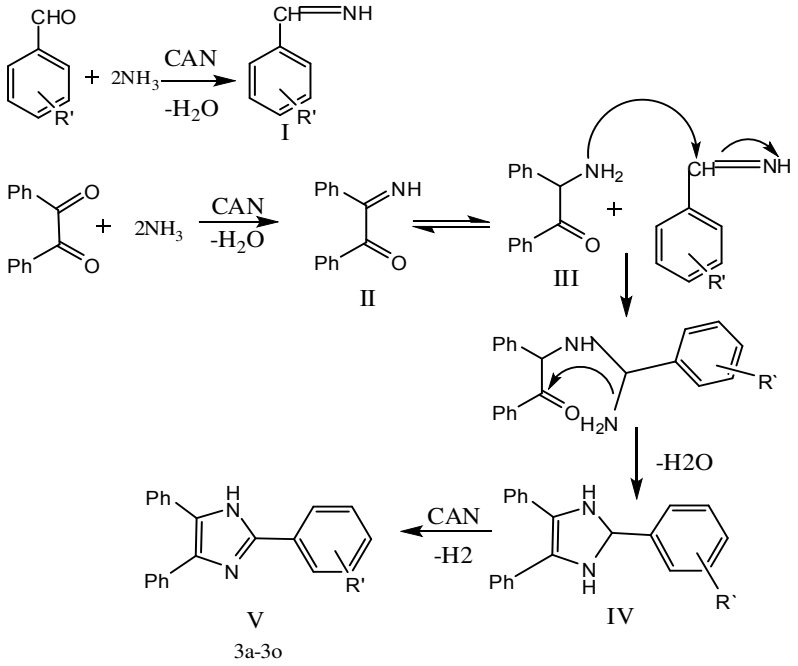
[a] Entry 1-6

[b]CAN Ceric ammonium nitrate [$(NH_4)Ce(NO_3)$], ND [c] no product formation, [d] isolated yield 1a(benzil) 1b(benzoin) obtained by column chromatography.

Ammonium acetate is a solid source of ammonia which can be conveniently generated in situ through the dissociation of ammonium acetate. Usually, the amount of ammonium acetate used is loosely controlled. A large excess is often used for two reasons one is that it is water soluble and excess amount can be easily removed during a work up and secondly it is a neutral salt and not a significant active species other than as an ammonia source. .

[a]Entry	Catalyst	Amount (mol%)	Time(hrs)	Yield(%)[d] 1a	1b
1	NO	-	5	ND[c]	ND[c]
2	CAN	5	5	90	91
3	CAN	10	5	75	78
4	CAN	20	5	73	70
5	CAN	25	5	85	87
6	CeSO4	20	7	60	58

TABLE 2: Synthesis of 2,4,5 trisubstituted imidazoles 3a-3o:



Scheme 2 Plausible Mechanism For The Formation Of Triarylsubstituted Imidazole

According to the literature survey it was reported that Balalai et.al [18] and Qing Xiang Guo [24] ,synthesized 2,4,5 trisubstituted imidazole by using benzoin(1b), zeolite HY and Sio_2 respectively in microwave irradiation in our methodology we were reported the formation of imidazole by using directly benzoin(1b)with the same reaction condition schem-1.The benzoin(1b) reflux with acetic acid and the product was not found even after 24 hrs. When we used CAN a powerful oxidizing reagent (schem 1) we found very good results summarized in table 2. The CAN has promoted this heterocyclization reaction by virtue of its inherent bronsted acidity which makes it capable of bonding with the carbonyl oxygen increasing the relativities of the parent carbonyl compounds. The CAN promotes the splitting of ammonia required for the initial condensation.

For the postulated mechanism starting from 1,2-diketone schem 3.The CAN may facilitate the formation of a amine intermediate I, which under Bronsted acid catalysis of the CAN condenses with the carbonyl carbons of the 1,2-diketone followed by dehydration to afford the imino intermediate II ,which rearranges to the required the tri-aryl imidazole III . A probable mechanism for the synthesis involving benzoin schem 3 .It is highly probable that the Bronsted acidity of the CAN may have promoted the formation of α-amino ketone II , aryl aldimine I their subsequent condensation and intermolecular cyclization to the Imidazoles III, which dehydrogenates to the triaryl Imidazoles V. It was thought that the dissolved oxygen in the CAN may have brought about the formal oxidation of the imidazole.

3. CONCLUSION:

In conclusion, we have developed an efficient, convenient and one-pot protocol for the synthesis of biologically potent 2,4,5-triaryl imidazoles via the condensation of aromatic aldehyde and benzil or benzoin with ammonium acetate using ceric ammonium nitrate. The process give rise to excellent isolated yield of triaryl imidazole .The study of antimicrobial activity is under progress.

4. EXPERIMENTAL:

All reported yields are isolated yields. Melting points are uncorrected and were recorded by open capillary.Infra red spectra were recorded with ATI MATT-SON RS-1 FTIR spectrometer in (KBr) .`HNMR spectra were recorded on a Bruker AC-200 (MHz) spectrometer in $CDCl_3$/DMSO-d6, with TMS as an internal standard.

General Procedure For Synthesis Of 2,4,5-Triaryl Imidazoles From 1,2-Diketones (1a)Or A-Hydroxyketone(1b)

A mixture of 1,2-diketones (1a) or the a-hydroxyketone (1b) (1 mmol), substituted aldehydes (2a-h,1mmol), ammonium acetate (10 equiv) and CAN (10mol%) was reflux at 75°C for the appropriate time mentioned in Tables 2. The completion of reaction was monitored by TLC using ethyl acetate: petroleum ether (1:9). After completion of reaction, the reaction mixture was diluted with water. The solid imidazole products, which separated out, were filtered, washed with sodium bisulphate and dried. The crude products, thus isolated, were pure (single spot on TLC). They were subjected to further purification by column chromatography 10% EtOAc in petroleum ether used as eluent to yield the desired substituted imidazoles in excellent yields of 86-92%

5. AKNOWLEGDMENT: Author thankful to the Department of Chemistry, B.Raghunath ACS College, Parbhani for providing facilities.

SPECTRAL DATA:

2-(4,5-Diphenyl-1*H*-imidazol-2-yl)-6-methoxy phenol(3a):
MP 168°C; IR ((cm^{-1})) .730,1234,1210,1654, 2920,3512,3600; 'HNMR (($CDCl_3$/DMSO-d_6, 200 MHz) δ: 3.86 (s, 3H), 6.32-5.45 (m, 3H), 7.22-7.12 (m, 5H), 7.40-6.95 (m, 5H), 12.4 (brs, IH); ^{13}C NMR (CDCl,/DMSO-d_6, 200 MHz) 544.3, 110.9, 112.1, 155.6, 117.1, 126.3, 125.6, 122.1, 126, 1

2-(4-Methoxy-phenyl)-4,5-diphenyl-l*H* -imidazole (3b):

Mp 220 °C; IR ((cm^{-1})) 1212, 1600, 2260, 2893. 3420; 'H NMR ($CDCl_3$/DMSO-d_6, 200 MHz) δ: 3.85 (s, 3H), 6.93-6.60 (d, 7 = 8.8 Hz. 2H), 7.10-7.02 (m, 10H), 8.16-8.12 (d, ,J=8.7 Hz, 2H). 12.39 (brs, IH); ^{13}C NMR (CDCl d_6/DMSO-d_6, 200MHz) *5* 48.7, 111.2, 120.7, 126.3, 126.5, 127.3, 127.4, 132.8, 145.7,

2-(4,5-Diphenyi-l *H* -imidazol-2-yl)-2-methoxy phenol (3c):
Mp 195 °C; IR ((cm^{-1})) 1240, 1470, 1620, 2910. 3510, 3614; 'H NMR ($CDCl_3$/DMSO-d_6, 200 MHz) δ: 3.80 (s, 3H), 6.75-6.69 (d, 7 = 8.22 Hz, IH], 7.11-7.19 (m, 5H), 7.22-7.23 (d. 7 = 8.1 Hz, IH), 7.40-7.45 (m, 5H), 7.55-7.56 (d, 7= 8 Hz, IH), 12.52 (brs, IH); ^{13}C NMR (CDCl /DMSO- d_6 200 MHz) *d* 55.1, 108.5, 114.6, 118.1, 121.1, 126.2. 127.3, 127.5, 132.3, 146.3, 146.8.

2-(4,5-Diphenyl-l *H* -imidazol-2-yl)-phenol (3d):
Mp 203-205 °C; IR ((cm^{-1})) 1211, 1608, 2500. 2953. 3475, 3696; 'H NMR ($CDCl_3$/DMSO-d_6, 200 MHz) δ : 6.87-6.95 (d, J=7.5 Hz, 2H), 6.96-7.01 (d, ,J = 8.06 Hz, 2H), 7.17-7.23 (m, 10H). 12.74 (brs, IH): ^{13}C NMR ($CDC1_3$/DMSO- d_6, 200MHz) *d* 112.7, 116.4, 118.1. 124.8, 127.4, 127.8, 129.1, 145.7.

4-(4,5-Diphenyl-l *H* -imidazol-2-yl)-phenol (3e):
Mp 230-231°C; IR (cm^{1}) 1216. 1638, 2465, 2998, 3432, 3596; 'H NMR ($CDCl_3$/DMSO-d_6, 200 MHz) δ:
6.97 (d, *J*= 8Hz, 2H), 7.52-7.87 (m, 10H), 7.88-7.92 (d, J = 8.5 Hz. 2H), 12.58 (brs, IH); ^{13}C NMR ($CDCl_3$/DMSO-d_6, 200MHz) *d* 111, 117.6, 124, 123.3, 120.1, 122, 140.

2-(4-Methyl-phenyl)-4,5-diphenyl-l*H* -imidazole (3f):
Mp 158-161 °C IR(cm^{-1}) 1215, 1453, 1486, 1496, 1601, 2926, 'H NMR ($CDCl_3$/DMSO-d_6, 200 MHz) δ:2.30 (s, 3H), 7.41-7.51 (d,.10H), 7.29-8.52 (d, 4H), 13.58 (s,1H) ^{13}C NMR (CD Cl_3/DMSO-d_6, 200MHz) 48.8, 126.5, 127.1, 128.3, 128.8, 129.5, 130.7, 134.4, 138.2, 147.3.

2-(3-Nitrophenyl)-4,5-diphenyl-1*H*-imidazole (3g):
Mp 198-200 °C IR(cm^{-1}) 1446.3, 1533.8, 1540.7, 1602.6, 3058. 'H NMR ($CDCl_3$/DMSO-d_6, 200 MHz) δ:13.11 (s,1H), 8.98 (s, 1H), 8.53 (d, j=9Hz 1H), 8.22 (d, j=9Hz, 1H), 7.76 (t, 1H), 7.25-7.5 (m, 10H) ^{13}C NMR (CD Cl_3 /DMSO-d_6, 200MHz) 122.8, 123.9, 127.5, 127.6, 128.7, 129.2, 129.3, 130.1, 131.5, 133.6, 138.2, 148.4, 177.1.

2-(4-Dimethylaminophenyl)-4,5-diphenyl -1*H*-imidazole (3h):
Mp 237-240 °C IR(cm^{-1}) 1445.7, 1508, 1551, 1661, 2919.1, 3057,8 . , 'H NMR ($CDCl_3$/DMSO-d_6, 200 MHz) δ: 2.98 (s, 6H), 6.78-7.92 (m,14H), 13.56 (s,1H). ^{13}C NMR (CD Cl_3 /DMSO-d_6, 200MHz) 112, 121.3, 126.9, 127.1, 127.3, 127.8, 127.9, 128.2, 128.3, 129.4, 129.5, 134.5, 145.1, 150.1

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Green Chemistry Approaches Are The Need Of The Hour

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Abstract: *All over the world there is a severe problem of environmental pollution. Therefore* medicinal */organic chemists also develop synthetic protocols, which follow principles of green chemistry.New drug will be selected on the basis of virtual screening based on computer aided drug designing, development and discovery (CADDD) followed by their synthetic procedure which should maintain atom economy preferably through multi component reaction free from hazardous solvent, should consume less energy i.e. supported by grinding technique, micro-wave or ultrasound irradiation with excellent yield of the product. In short a procedure should be environmentally benign.Even chemistry practicals hould be conducted on micro scale technique in universities and colleges to avoid environmental pollution. We wish to present here with a brief elaboration of such procedures for selection of good leads and synthesis of various compounds.*

Keywords: *Green Chemistry, CADDD, Multicomponent Reaction, Micro scale chemistry*

1. INTRODUCTION:

All over the world there is a severe problem of environmental pollution. Therefore, medicinal/organic chemists also develop synthetic protocols, which follow principles of green chemistry.Green Chemistry[1] is a philosophy of chemical research and engineering that encourages the design of products and processes that minimize the use of and generation of hazardous substances. Green Chemistry can be comprehensively illustrated as a set of 12 principles. These principles include instructions for chemists concerning the creation of new substances, new syntheses and new technological processes. These principles are

1.1-Prevention

It is better to prevent waste than to treat or clean up waste after it has been created.

1.2-Atom Economy

Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.

1.3-Less Hazardous Chemical Syntheses

Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.

1.4-Designing Safer Chemicals

Chemical products should be designed to achieve their desired function while minimizing their toxicity.

1.5-Safer Solvents and Auxiliaries

Unnecessary use of auxiliary substances (e.g. solvents, separation agents, etc.) should be avoided wherever possible and made innocuous when used.

1.6-Design for Energy Efficiency

Energy requirements of chemical processes should be recognized for their environmental and economic impacts and should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure.

1.7-Use of Renewable Feed stocks

Whenever technically and economically practicable, raw material or feedstock should be renewable rather than depleting it.

1.8-Reduce Derivatives

Unnecessary derivatization (use of blocking groups, protection/deprotection and temporary modification of physical/chemical processes) should be minimized or avoided if possible, because such steps require additional reagents and can generate waste.

1.9-Catalysis

Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

1.10-Design for Degradation

Chemical products should be designed so that at the end of their function theydo not persist in the environment and break down into innocuous degradation products .

1.11-Real-time analysis for Pollution Prevention

Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control, prior to the formation of hazardous substances.

1.12-Inherently Safer Chemistry for Accident Prevention

Substances and the form of a substance used in a chemical process should be chosen so as to minimize the potential of chemical accidents, including releases, explosions, and fires.

These principles can motivate chemistry at all levels: research, reduction to practice, education, national and international policy, and public perception. In other words, green chemistry is aboutthe redevelopment of chemistry to protect life itself.

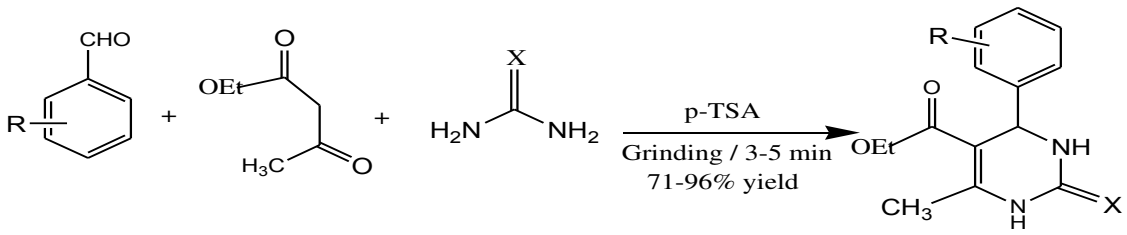
2. GREEN METHODS:

The development of cleaner protocolshas become a crucial and demanding area in modern organic synthesis[2-4].The most commonly used environmentally benign approaches are discussed here.

2.1-Grinding Technique

Grindstone technique has been considered as a clean and useful protocol in organic synthesis over the last few decades. In this technique, reaction occurs through generation of local heat by grinding the solidreactants using mortar and pestle. Reactions are initiated bygrinding, with the small amount of energy through friction. The grinding reactions are simple to handle, reduce pollution, comparatively cheaper to operate and may be regarded as more economical and ecological.

Ajay K. Bose *et al* [5]synthesized tetrahydropyrimidinones via the multi-component Biginelli reaction under solvent-free conditionsusingGrindstone Chemistry in presence of p-toluene sulfonic acid(p-TSA) as catalyst. The reagents were ground together in a large glass or porcelain bowl by using a hand held electric food mixer with stainless steel rotors, to conduct the reaction on large scale. For better understanding of the energetic of reactions, a thermocouple connected to a computer was used for recording the Reaction Temperature Profile **(Scheme 1)**.



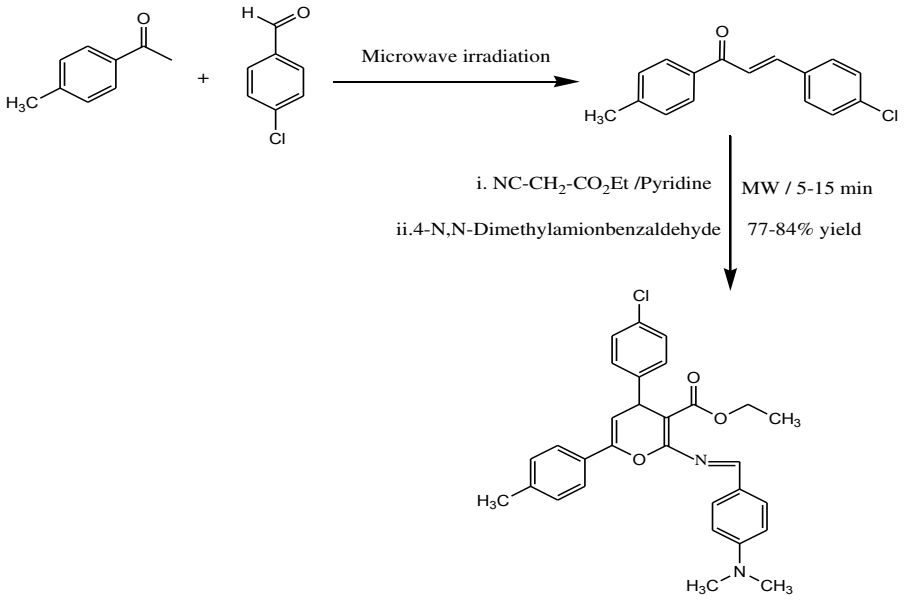
Scheme-1

Nazeruddin *et al* [6]reported the same reaction using grape juice as a catalyst by grinding technique only.

2.2-Microwave

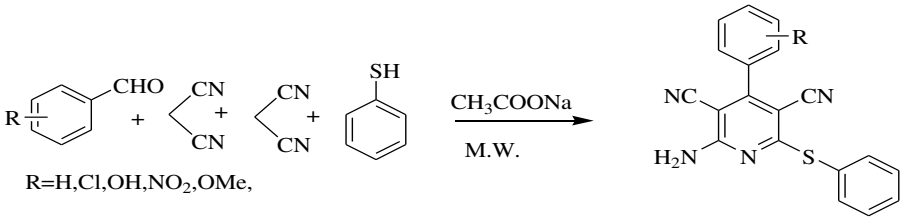
Microwave assisted organic reactions constitute an emerging technology that makes experimentally and industrially important organic synthesis more effective and more environment friendly than conventional thermal methods. Microwave as non-thermal energy transfer source is well known to enhance reaction rates, yields and selectivity in organic synthesis and has found wide applications in synthetic organic chemistry.

Subal Debnath *et al*[7]synthesized Ethyl2-amino-4-(4-chlorophenyl)-6-(4-methylphenyl)-4H-pyran-3-carboxylate and their Schiff's bases by conventionaland microwave methods. The required α, β - unsaturated ketones (chalcones) were prepared by the Claisen-Schmidt reaction. The chalcone, (2*E*)-3-(4-chlorophenyl)-1-(4-methylphenyl)-prop-2-en-1-one, prepared from acetophenone and 4-chlorobenzaldehyde, was treated with ethyl cyanoacetate in pyridine to prepare pyran which was then converted to pyran Schiffs bases with 4-N,N-dimethylaminobenzaldehyde. All the new compounds werescreened for anti-bacterial and antifungal activities **(Scheme II)**.



Scheme-II

Nazeruddin et al [8] investigated a sodium acetate (10 mol %) catalyzed, one-pot simple and efficient procedure for the rapid construction of substituted pyridines via a three-component reaction of aldehydes (1mmol), malononitrile(1.1mmol) and thiophenols (1mmol) in Methanol under microwave irradiation (62-92%)(Scheme III).

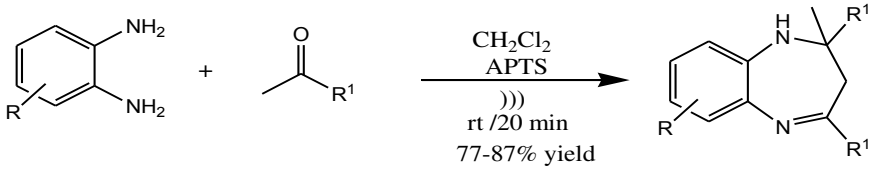


Scheme-III

2.3- Ultrasound

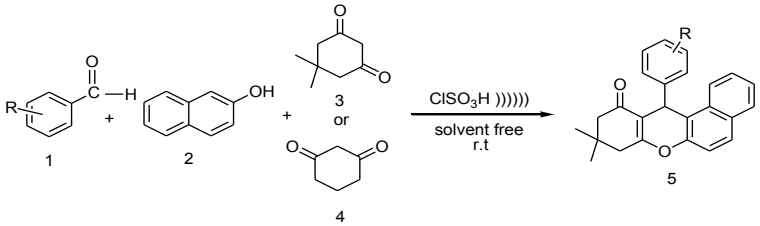
Ultrasound irradiationhas been considered as a clean and useful protocol in organic synthesis as compared with traditional methods. A large number of organic reactions can be carried out in higher yield, shorter reaction time and mild reaction conditions under ultrasound irradiation.This technique is more effective in terms of energy conservation and waste minimization taking green chemistry concepts into account.

He lio A. Stefani*et al* **[9]**synthesized 1,5-Benzodiazepines by a reaction of o-phenylenediamines with variety of ketones by ultrasound irradiation in presence of APTS (p-toluenesulfonic acid). The condensation occurred in a mild condition with good to excellent yields.It was observed that this is a general method that tolerates bothelectron-withdrawing and electron-donating groups inthe diamine **(Scheme-IV)**.



SchemeIV

Abdul karim Alkadasi [10] investigated the activity of Chlorosulphonic acid as a catalyst in the synthesis of xanthene derivatives by condensation of aromatic aldehydes **1**, β-naphthol **2**, 5, 5-dimethyl-1, 3-cyclohexanedione **3** and 1, 3-cyclohexanedione **4** (scheme1).under ultrasound and solvent free conditions Sscheme-V

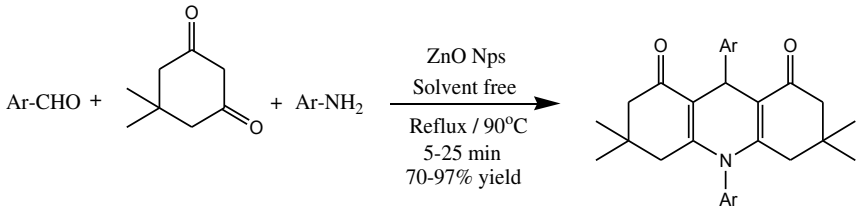


Scheme-V

Nanoparticles as a catalyst

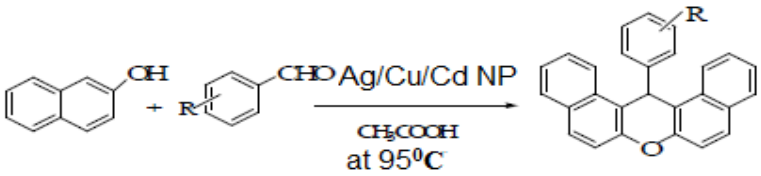
Last decade has witnessed significant growth in the field of nanoscience and nanotechnology. The applications of nanoparticles (NPs) in organic catalysis have attracted considerable attention because of their improved efficiency and mild reaction conditions. These materials provide enormously large and highly reactive surface area henceexhibit some unique behavior in comparison to bulk materials.

Javad Safaei-Ghomi *et al* [11]demonstrated the use of ZnO nanoparticles as a highly effective and readily recyclable catalystfor the one-pot synthesis of 1,8-dioxo-decahydroacridinesand 1,8-dioxooctahydro-xanthenes *via* multi-component reactionsunder solvent-free conditions. The presented method is mild, green and cost effective to afford theproducts in good to excellent yields **(Scheme V)**.



Scheme-V

Y.I.Shaikh *et al* [12] developed Ag, Cd and Cu nanoparticles catalysed one pot synthesis of 14-Aryl -14-H-dibenzo [a, j] xanthene (Scheme 1) by condensation of various substituted aldehydes and β- napthol using acetic acid as solvent under reflux. This methodology has several advantages such as inexpensive catalyst, easily available reactant, shorter reaction time and products with excellent yields. Further the catalyst can be recovered by filtration and reused for four cycles with almost consistent activity **(Scheme VI)**.



R= H, 4-Cl, 2-Cl, 4-NO_2, 4-OCH_3

Scheme-VI

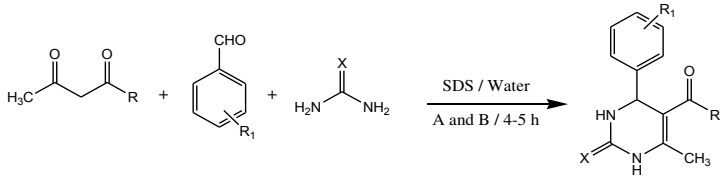
2.5 Green Solvent

Solvents are consumed in large quantities in chemical and pharmaceutical industries for syntheses as well as for cleaning and degreasing.The traditional solvents are often toxic and it has been observed that majority of waste and pollution is directly related to solvents.Taking into account the impact of solvents on the environment, safety and health issues, the search for green solvents has become a great challenge in organic synthesis. The idea of green solvents expresses the goal to minimize the environmental impact resulting from the use of solvents.

2.5.1-Water

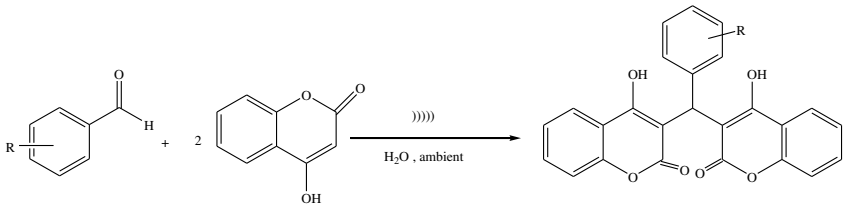
Water is universally a greener solvent in terms of availability, low cost, safety and environmentally benign in comparison with organic solvents.Moreover, water is a renewable resource which is in agreement with one of the principles of green chemistry. In this context, many researchers employed water as a reaction medium in organic synthesis.

Beda Durga Prasad *et al* [13]recentlydisclosed a simple, green and efficient procedure for the synthesis of 4-aryl-3,4-dihydropyrimidine-2(1*H*)-ones/thione via Biginelli condensation from 1, 3-dicarbonyl compound, substituted aldehydes and urea / thiourea by a novel catalyst Sodium Dodecyl Sulphate (SDS), in aqueous media. The products obtained in excellent yields under both conventional and domestic microwavemethods**(Scheme-VII)**.



Scheme-VII

Abdul Karim Alkadasi ***et al***[14] reported ultrasound assisted catalyst free synthesis of bis coumarins in water (Scheme-VIII)



Scheme-VIII

2.7 Computer Aided Drug Design Development and Discovery (CADDD):

Estimates of time and cost of currently bringing a new drug to market vary, but seven–twelve years and $ 1.2 billion are often cited. Furthermore, five out of forty thousand compounds tested in animals reach human testing and only one of five compounds reaching clinical studies is approved. This represents an enormous investment in terms of time, money and human and other resources. It includes chemical synthesis, purchase, and biological screening of hundreds of thousands of compounds to identify hits followed by their optimization to generate leads which requiring further synthesis. In addition, predictability of animal studies in terms of both efficacy and toxicity is frequently suboptimal. Therefore, new approaches are needed to facilitate, expedite and streamline drug discovery and development[15], save time, money and resources. It is estimated that computer modelling and simulations account for ~ 10% of pharmaceutical R&D expenditure and that they will rise further in coming years. Role of computational models is to increase prediction based on existing knowledge . Computational methods are playing increasingly larger and more important role in drug discovery and development and are believed to offer means of improved efficiency for the industry . They are expected to limit and focus chemical synthesis and biological testing and thereby greatly decrease traditional resource requirements. Modern drug discovery and development process including prominent role of computational modeling and commonly used computational approaches are ligand-based design (pharmacophore)[16], structure (target)-based design (docking)[17], and quantitative structure-activity/property relationships (QSAR/QSPR) (computational predictive toxicology)[18]This approach is indirectly a green chemistry approach and nohing but an virtual screening.

Various new analogues of diclofenac were designed by ***Osman et. al***. [19]and their physiochemical properties such as log P, HOMO, LUMO and pKa etc. were calculated and out of them five compounds were selectedby comparing with diclofenac and for synthesis petasis reaction was exploited,which is multicomponent reaction.Docking studies were performed using (Auto Dock 4.2.) 2006.02 (CCG Inc.20) and runs on a cluster of 12 Pentium IV processors, the results were in accordance with the biological evaluation.

2.7 Microscale Chemistry:

Microscale chemistry (often referred to as small-scale chemistry)**[**20,21], is an analytical method and also a teaching method widely used at school and at university levels, working with small quantities(milligrams) of chemical substances. Small-scale working takes place with low-cost and even no-cost material. There has always been a place for small-scale working in qualitative analysis. In various European universities and colleges including United State of America, South Africa,Japan,China Thialand and Kuwait. Micro scale chemistry is commonly used as a teaching method.However in India microscale chemistry is adopted as a teaching method by few universities only.As per the latest statistics from the UGC website, as of February 2017, there are **789** universities,**37,204** colleges and **11,443** stand-alone institutions in India. If in India, small scale chemistry/ micro scale chemistry is implemented in all universities and colleges lot of chemicals and material used for making apparatus can be saved. Further, a student is not increasing the pollution.This is nothing but a great green chemistry approach.

2.8 Conclusion:

All the research scholars have to follow the principals of green chemistry in carrying out their research program. All the pharmaceutical industries should select the novel drugs by virtual screening to save the time and money followed by synthesis preferably through some multi component reaction then evaluation of the novel drug may be carried out in vitro and vivo. last but not the least all the chemistry students of various universities colleges should carry out their chemistry practical on micro scale level only. Everybody has to do it religiously to protect our planet from various pollutants.

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Review Article Of Metal Oxide Electrode Materials For Supercapacitor Application

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Abstract: *In the electrostatic field one of the major issues is storage. In the recent years the need of alternate or non-conventional energy sources with high density and power has been tremendously increased. Supercapacitor is one of the promising energy storage devices which possess high specific capacitance, high power density, long life cycle. The performance of supercapacitors is determined by its electrode material. Among the various supercapacitor electrode materials, recent research focuses on synthesis of transition metal oxides/ hydroxides, carbon metals and polymers. In this paper, we present review of metal oxide materials which can be used as supercacitor electrodes and widely used in supercapacitor devices. We also discuss the synthesis and characterization techniques evolved in supercapacitor studies.*

Key words: *supercapacitor, Carbon nanomaterial, pseudocapacitors, X-ray.*

1. INTRODUCTION:

With the increasing fuel problems, environmental pollution and global warming there is a strong need to develop clean, efficient and sustainable energy source for storing energy when it is available and retrieving when it is needed [1-2]. There are many applications such as stand-by power systems, cell phones, and electric hybrid vehicles where electric energy storage is necessary [3]. Supercapacitors, also known as Ultracapacitor, electrochemical capacitors or double layer capacitors, utilize high surface area electrode materials and thinner dielectrics to achieve greater capacitances and energy density than that of conventional capacitors and greater energy density than that of batteries [4-7]. Supercapacitors can be used in various energy storage devices, either stand-alone or in combination with batteries. Supercapacitors reach 20 times higher than that of batteries power density (1 kW/kg) and better life cycle, it can be charged and discharged rapidly [8-9].Fig in Ref. [10] shows the comparison between specific power and energy for different electrical energy storage devices. This plot indicates that supercapacitors occupy a region between conventional capacitors and batteries. Supercapacitors are driven by the same basic principle of conventional capacitors but they utilize higher surface areas and thinner dielectrics that decrease the distance between the electrodes. The Capacitance 'C' is directly proportional to the surface area 'A' and inversely proportional to the distance 'D' between the electrodes:

$$C = \varepsilon_o \varepsilon_r \frac{A}{D}$$

Where, ε_r the electrolyte dielectric constant, ε_o is the permittivity of a vacuum [11]. The stored energy E in a supercapacitor depends upon specific capacitance (C) and the operating voltage (V) [12] given by:

$$E = \frac{1}{2} CV^2$$

The maximum power Pmax depends on the voltage and the internal resistance R as follows:

$$Pmax = \frac{V^2}{4R}$$

Generally the mechanism of the supercapacitors divided into three categories based on energy storage and cell configuration: (i) Electric Double- Layer Capacitors (EDLC's), (ii) Pseudocapacitors and (iii) Hybrid capacitors as shown in Figure

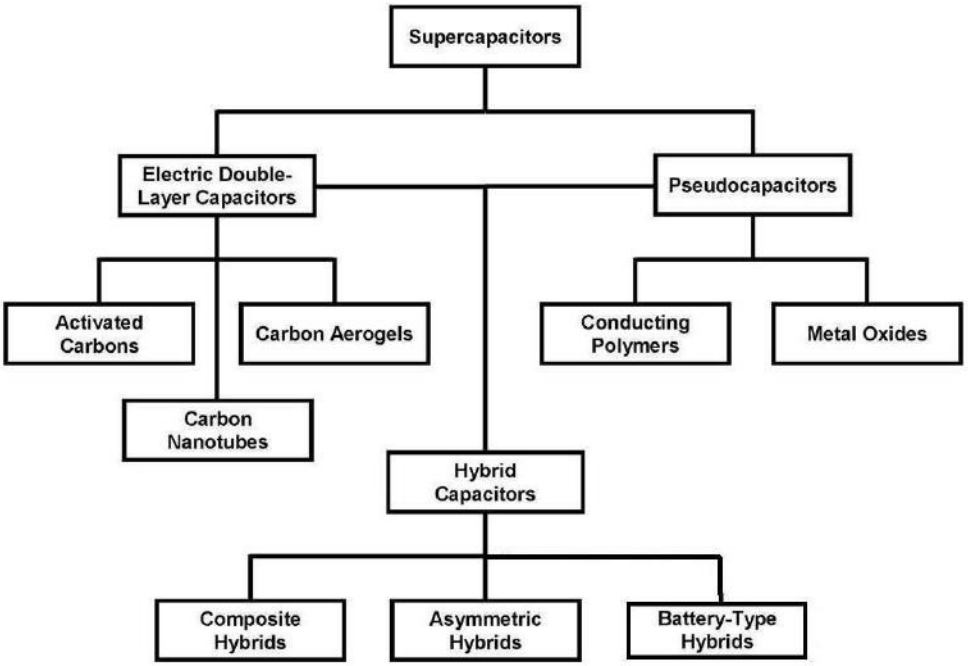

Figure: Classification of Supercapacitor

Electric double-layer capacitors

Electrochemical double-layer capacitors (EDLCs) are constructed from two carbon-based electrode material and separated by insulator. It stores the energy charge by non-faradaic manner; the charge storage mechanism is based on the electrostatic charge accumulation at the electrode-electrolyte interface [13]. The most common electrode material is activated carbon. Carbon nanomaterials are having unique structures with large surface area, better electrical conductivity, high chemical & mechanical stability easy to process and It is cheap. The specific capacitance in carbon-based electrode materials is less and hence achieving a high energy density has become a difficult task in EDLC's.

Pseudocapacitors

Pseudo-capacitors electrostatically store the charge as compared to EDLC's and the faradaic charge transfer occurs at electrode-electrolyte interface [14]. It has high specific capacitance and high energy density than the electrical double layer capacitance due to Faradic process. Transition metal oxides [15] and conducting polymers [16] are mainly used as pseudocapacitor electrodes. The main disadvantage of the pseudocapacitors is low power density [17].

Hybrid capacitors

EDLC's offers large power performance and good cyclic stability while pseudocapacitors possess greater specific capacitance and energy densities. Hybrid supercapacitors offer a high energy density and fast charging rate in the same cell [18]. The combination of two different electrodes typically results in more energy storage due to the wider operating voltage of an organic electrolyte and the good specific capacity of the battery type electrode. Hybrid capacitors have been tested with both positive and negative electrodes in aqueous electrolytes to improve the performance [19]. There are three subcategories on the basis of configurations of electrodes (a) composite, (b) asymmetric and (c) battery-types.

Metal Oxide Based capacitors

Over the past few decades many advances have been made in the area of preparation of nano materials. Metal oxides such as RuO_2, MnO_2, NiO, In_2O_3, Co_3O_4, V_2O_5, Fe_3O_4, Bi_2O_3, IrO_2, $NiFe_2O_4$, $BiFeO_3$ etc) are promising material for the fabrication of high energy densities devices called supercapacitors due to their exceptional physic-chemical properties [20-21]

Ruthenium oxide

Among the various metal oxides amorphous RuO_2 is a promising electrode material with excellent high electrochemical capacitance theoretically ~2000 F/g, high electrical conductivity, long cycle life and good electrochemical reversibility [22] which has various forms like nano-porous film [23] nanoneedles [24], and

nanoparticles [25]. The highest specific capacitance among seudocapacitive materials, about 1000F/g [26]. Ruthenium Oxide formed by sol–gel and electrodeposition methods exhibits large capacitance of 720 and 788 F/g, respectively [27,28]. Particles which are small, uniform in size, and highly dispersed on a carbon surface, prepared with the polyolmethod, exhibit specific pseudocapacitance of 914F/g [29]. Hu et al [30] have synthesized nanotubular array of RuO2. xH2O by template method which exhibited a very high capacitance value of about 1300 F/g. Amorphous ruthenium oxide materials in the H2SO4 electrolyte exhibited a maximum capacitance of 720 F/g upon calcination at 150°C. For a crystalline state in a KOH electrolyte, a maximum capacitance of 710 F/g was obtained by calcinating ruthenium oxide at 200°C [31]. Specific capacitance of 710 F/g in a KOH electrolyte was reported for a SnO2–RuO2 composite electrode wherein RuO2 was deposited by an incipient wetness precipitation method.

Manganese oxide

Manganese oxide (MnO_2) has also been used as an electrode materials for supercapacitor applications which shows all-around good performance. Manganese oxides found to be an alternative to RuO2 because of their relatively low cost, low toxicity, and theoretical high capacitances value 1100–1300F/g [32–36].

Cobalt oxide

Cobalt oxide (Co3O4) has a cubic structure and most studied material due to their high electrical conductivity, excellent reversible redox behavior and long-term stability. Theoretical capacitances value of Co_3O_4 exhibits up to 3000 F/g [37]. Nanowire grown by CVD method shows specific capacitance of 1100 F/g[38]

Other Metal Oxide

Other than RuO2, MnO and Co3O4 electrodes, zinc oxide (ZnO), Vanadium oxide, tin oxide (SnO2) and iron oxides (Fe2O3 and Fe3O4) and Nickel oxide (NiO) have been studied for supercapacitor electrode materials. Lee et al., have reported the prepared amorphous V2O5 exhibits a maximum specific capacitance of 350 F/g [39].Amorphous SnO2 synthesized by electrochemical deposition method which shows specific capacitance of 285 F/g [40]. Recently, a Fe2O3 film has been prepared via a hydrothermal method which exhibited a specific capacitance of 118.2 F/g[41]. Nickel oxide (NiO) is also suitable for pseudocapacitor electrode applications as the theoretical specific capacitance is up to 3750 F/g [42].

2. SYNTHESIS TECHNIQUES:

Anodization method

An electrochemical method known as anodization or anodic oxidation is a well-established surface modification technique for metals to produce protective layers. In this process an oxide (anodic) layer is chemically built on the surface of the metal. This method is used for preparing metal oxide nano tubes/rods, where different anodization conditions can be used to control diameter, pore size, morphology, surface functionality, etc.

Electrodeposition method

Electrochemical deposition is a very attractive and well known method due to inexpensive, simple and effective process of fabrication of metallic coatings. Also the electrodeposition can made a wide range of nanostructured materials. While electrodeposition continues to be widely used for protective or decorative coatings, challenging new applications have been found in the electronics industry, particularly exciting developments include the development of thin film magnetic recording heads for hard disks, and the recent replacement of aluminum and its alloys by electrodeposited copper for interconnects in ultra large scale integrated circuits.

SILAR method

The Successive Ionic Layer Absorption and Reaction method is used to create thin films from a variety of different substrates and to produce different coatings for applications, including solar panels and semiconductors. The SILAR method is a chemical bath solution method that is an extension of the similar chemical bath thin film production method. The main advantages of the SILAR deposition method include the ease of completing the method and the relative low cost. For small amounts of substrates to be treated using the SILAR method, the process can be completed using glass beakers. The ease of application allows the thickness of thin films created using the SILAR method to be controlled more easily than in other applications.

Chemical Bath Deposition method

Chemical bath deposition (CBD) is a one of the cheapest method to deposit thin films and Nanomaterials, as it does not depend on expensive equipment and is a scalable technique that can be employed for large area batch processing or continuous deposition.

3. CHARACTERIZATION TECHNIQUES:

X-ray diffraction

This technique is used for the structural characterization of the sample. X-ray diffraction patterns were recorded using Cu-Kα radiation (1.54A0). It is useful for identifying crystal structure of materials. Thus crystalline phases existing in the materials were identified by comparing structural features with standard JCPDS data.

Uv-Visible Absorption Spectroscopy

To determine the formation of nanoparticles optical absorption spectroscopy is used. Absorption spectra were recorded using a UV absorption spectrometer, from this we can calculate band gag of materials.

Scanning Electron Microscopy & Energy Dispersive spectroscopy

This technique is useful for understanding the surface structure of a sample and to explain the phenomena occurring on a micrometer (μm) or sub-micrometer scales to study microstructure, grain size, surface morphology etc.

Energy Dispersive X-ray Analysis

Energy dispersive X-ray analysis (EDX) is a powerful technique for the compositional analysis of the thin film samples. The EDX setup experimentally employs an energy-dispersive X-ray spectrometer and is a part of an electron microscope.

Cyclic Voltammetry

Cyclic Voltammetry (CV) is an electrochemical technique which measures the current that develops in an electrochemical cell under conditions where voltage is in excess of that predicted by the Nernst equation.

4. CONCLUSION:

Supercapacitors have emerged as an alternative solution in energy technology with excellent electrochemical properties, high energy density and good cyclic stability. Due to the high surface area, high thermal and electrochemical conductivity it can be used in many application such as specific power systems and also there has been great interest in developing supercapacitors for electric vehicle hybrid power systems, back-up and emergency power supplies and pulse power applications. It is one of the major areas that require further research and development to become supercapacitors as a realistic power solution for an increasing number of applications.

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Physico Chemical Analysis Of Well Water In Kothure Village-Niphad-Nashik – Maharashtra (India)

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Abstract: *Physico-chemical analysis of the well water samples of Kothure Village of Niphad Tahsil, Nashik District has been studied for various parameters. This analysis includes pre-monsoon (May) and post-monsoon (September) periods. All the water samples were analyzed to access the water quality parameters like Temperature, ph, Turbidity, Chloride, Hardness, Total Dissolved Solids (TDS), Sodium, Potassium, Alkalinity, Nitrates, Dissolved oxygen (DO), Electrical conductivity, Magnesium, Calcium, Phosphate etc. It was found that the parameter values are more in pre-monsoon period than post-monsoon period. The results indicates a lack of phosphate in water of Kothure Village.*

Key Words: *Physico-chemical, Well water, Pre-monsoon, post-monsoon, Phosphate.*

1. INTRODUCTION :

Water is an absolute necessity of life as well as universal solvent. It contains dissolved minerals and suspended particles even in its natural state. The quality of drinking water is rather a complex issue and involves various disciplines. Contamination results in several gastro-intestinal diseases. Pollution originated from contaminations of water with domestic sewage as well as from industrial wastes [1].

Water is one of the widely distributed resources on the earth. From the total quantity of water in the hydro-sphere only 1% water is available as fresh water, occurring in the form of Rivers, Lakes Streams (0.003%) and Ground water (0.61%) which can be used for human consumption provided its quality is suitable (A.K.De)

The chemical composition of water is ideally controlled by alteration of minerals in the rocks through the process of chemical weathering. The composition of water is highly variable depending upon climate, topography, geology, soil and other natural factors that across the region. Many early studies have attempted to interpret the composition of water in terms of above factors and the weathering reactions in the near surface environment (Vijay Kumar et al, 2004)

During recent decades however, in many parts of the decaan trap Hydrologic Province, continuing growth of population, industrial and agricultural activities have increased the pressure on the water resources to extent that numerous water bodies have become temporarily or permanently unsuitable for human health[2].

Although other scientific information exists about the status of water quality in restricted areas, very little scientific information is available regarding overall water quality. The role of water range of natural and human induced factors causing changes in the distribution and concentration of chemical constituents in the water is not clear also. Such information is very useful in locating suitable water resources for drinking water supply for agricultural planning and for industrial development.

According to WHO (1997) in most of countries the principal risk to human health associated with the consumption of polluted water are microbial in nature. Water quality deterioration may occur due to source of fecal pollution including grazing cattle, natural animal populations, septic tanks, failed sewage systems, recreational users and summer storm activity etc.

The quality of drinking water is a complex issue but is a vital element of public health. Poor water quality is responsible for the deaths of an estimated five million children annually. Due to the pressure of increasing populations and developing economy all over the world the present situation of water quality management is far satisfactory [3].

In view of this the present work was carried out in the Kothure Village (Niphad Tahasil), Nashik district of Maharashtra. The objective of this study was to assess the quality of drinking water in agricultural area severed by different sources from ground waters like tube wells and borings.

2. MATERIALS AND METHODS :

1) STUDY AREA:

Koture Village is located in Niphad tahasil, nearly 38 kilometers from Nashik city. Kothure Village is blessed with lot of water supply and very good climate and high quality soil. It is located on the bank of Godavari River which flows by the village. This village was chosen for this well water survey because this village was awarded as a 'Ideal Village' by Government of Maharashtra in 2005. The climate of Nashik district is characterized by dryness except in the

south-west monsoon season. The monsoon season is from June to September followed by the post monsoon season during October to November. Average rainfall of the district is between 2600 to 3000 nm. The maximum temperature in summer is 42.5 ^{0}C and minimum temperature in winter is less than 5.0 ^{0}C. Relative humidity ranges from 43% to 62%.

2) SAMPLE COLLECTION, PRESERVATION & STORAGE :

The samples were collected periodically to make periodic comparison i.e. before monsoon in the month of May 2008 and after monsoon in the month of September 2008.

The sample of irrigation water was collected in about 2000 ml plastic can. The container must be thoroughly cleaned before use and should be rinsed 3 to 4 times with the water which is to be examined. If the source of irrigation is tube well or hand pump then it is to be run for about 10 min. prior to sampling and for open well, several buckets of water have to be thrown out first. About half a liter of the sample is quite sufficient. The water sample after proper marking and labeling must be sent to the laboratory immediately for testing to avoid any change. If few days delayed is inevitable then 2 or 3 drops of pure Toluene may be added to prevent bacterial activity.

3) PHYSICO-CHEMICAL ANALYSIS*:*

Analysis of some water parameters such as Temperature, Colour, Odour, pH, Electrical conductivity and Fixation of DO were carried out at the sampling spots. Temperature was measured with the help of thermometer (110^0C), pH and electrical conductivity were measured with the help of portable water analysis kit. While DO was fixed by addition of MnO_2 (2 ml). Then the remaining parameters were tested in laboratory within 6 hours from the collection time.

3. RESULTS AND DISCUSSION:

Table 1 : Physico-chemical parameters of well water in Pre-monsoon period

Pre-monsoon																
Sr No.	**Temp. (^{o}c)**	**PH**	**EC (mhos /cm)**	**Acidity (mg /l)**	**Turbidity (ntu)**	**DO (mg/l)**	**Alkalinity (mg/l)**	**Cl (mg /l)**	**TDS (mg/l)**	**NO_3 (mg/l)**	**O-po_4 (mg/l)**	**Hardness (mg/l)**	**Ca (mg /l)**	**Mg (mg/l)**	**Na (mg/l)**	**K (mg/l)**
1.	28	7.76	552	20	0.9	4.0	200	55.30	353	61	00	118	32.06	9.25	133.5	1.50
2.	26	7.27	664	25	0.6	5.6	270	53.96	424	66	00	165	15.23	30.21	134	6.30
3.	28	7.55	784	15	1.3	5.2	280	80.94	478	64	2.934	120	32.86	9.21	122	5.40
4.	30	7.19	936	10	1.2	5.2	310	90.38	599	49	2.102	104	28.85	7.79	130	9.80
5.	27	7.32	1112	60	1.9	5.6	360	156.48	711	55	00	126	29.65	12.66	136	5.20
6.	27	7.41	1655	20	2.6	6.4	350	330.50	1059	57	00	112	32.86	7.30	117.2	16.77
7.	28	7.11	5434	35	7.9	6.0	710	1243.7	3477	47	00	542	180.36	22.41	135	16
8.	25	7.52	1349	30	2.3	6.8	330	245.52	363	42	0.949	50	10.42	5.84	84.1	17.70
9.	28	7.64	2327	80	5.5	4.4	520	391.20	1489	30	00	36	8.817	3.41	85	4.10
10.	27	7.27	2004	55	3.6	6.8	420	407.70	1282	46	1.167	122	29.65	11.69	127	17.90
11.	26	7.63	209	25	0.5	6.0	100	14.84	133	39	00	46	12.02	3.89	152	18.40
12.	24	7.57	348	40	1.5	4.4	180	29.68	223	44	3.224	124	32.86	10.23	118	20.10
13.	29	7.35	2251	25	4.0	5.6	530	438.43	1440	41	00	106	20.84	13.15	129	20.50
14.	25	7.54	3391	45	6.9	6.4	510	553.09	2170	44	1.642	172	24.84	25.33	158	16.80

15.	26	7.80	980	50	1.8	6.8	540	125.46	627	18	3.259	90	30.46	3.41	164	16.20
16.	29	7.55	3002	30	4.3	5.6	380	720.37	1921	49	00	168	28.05	23.81	121	6.80
17.	28	7.36	2374	40	4.5	4.4	370	586.82	1519	48	00	230	60.12	19.49	43	16.50
18.	30	7.10	4056	45	5.0	4.0	380	1139.9	2295	59	0.987	242	67.33	42.39	68	17.20
19.	28	7.70	2498	40	3.7	6.0	400	581.42	1598	48	00	94	31.26	3.89	64	3.20
20.	29	7.76	893	45	1.2	4.0	310	129.50	571	47	00	88	12.02	14.13	141	2.80
21.	28	7.49	1054	40	1.5	5.0	300	141.65	674	48	00	92	20.04	10.23	136	8.10
22.	28	7.35	883	45	2.0	6.8	320	94.43	565	43	00	70	21.64	3.89	132	3.90
23.	29	7.66	926	35	2.3	4.0	260	130.85	592	49	00	102	30.46	6.63	140	17.10
24.	26	7.87	492	20	0.9	7.6	240	33.73	341	47	00	90	24.84	6.62	54	5.80

Table 2 : Physico-chemical parameters of well water in Post-monsoon period

POST-MONSOON

SR. NO.	TEMP. (^{O}C)	PH	EC (mhos/cm)	ACIDITY (mg/l)	TURBIDITY (NTU)	DO (mg/l)	ALKALINITY (mg/l)	Cl (mg/l)	TDS (mg/l)	NO_3 (mg/l)	O-PO_4 (mg/l)	HARDNESS (mg/l)	Ca (mg/l)	Mg (mg/l)	Na (mg/l)	K (mg/l)
1.	21	7.20	1281	30	1.4	2.40	470	222.59	819	47	00	354	64.92	46.78	195	4.11
2.	22	7.14	1601	55	0.8	4.80	460	207.75	1025	49	00	322	71.34	35.08	230	9.21
3.	26	7.05	1297	20	1.2	2.80	460	134.90	830	48	00	360	65.93	47.75	187.4	11.27
4.	27	6.95	1160	15	1.5	1.60	450	149.74	742	40	00	304	52.90	41.90	170	15.70
5.	20	7.11	1354	70	2.2	3.60	480	199.65	864	42	00	366	53.70	56.52	257	12.30
6.	21	7.25	1400	30	3.1	2.80	480	205.05	896	43	00	312	65.73	36.05	148.3	34.81
7.	23	7.05	1756	45	8.1	4.40	860	1342.26	1124	38	00	650	197.9	38.52	241	36.02
8.	24	7.19	744	35	2.9	5.20	240	82.29	476	24	0.117	130	43.28	5.36	127.5	39.40
9.	20	7.10	680	95	6.0	1.60	210	71.50	435	10	0.081	116	32.86	8.284	139	12.05
10.	22	7.32	2267	65	3.9	2.40	520	407.40	1451	34	00	362	69.73	45.80	202	30.12
11.	22	7.36	719	25	4.0	4.00	230	83.64	460	24	1.497	126	36.87	8.771	290	26.87
12.	20	7.14	1695	50	0.7	2.40	510	280.59	1052	33	00	364	66.52	49.21	165	15.35
13.	23	7.05	1940	40	1.4	2.80	490	296.78	1241	23	0.036	306	76.95	27.77	205	36.87
14.	22	7.45	3577	50	4.6	5.20	610	454.61	2289	28	0.1044	484	95.30	59.93	210	19.11
15.	19	7.55	1332	55	7.2	4.80	330	196.95	846	3	00	248	53.70	27.77	236	23.30
16.	22	7.32	2870	40	2.4	1.60	340	671.80	2870	37	00	492	148.2	29.72	267	16.80
17.	22	6.98	3276	55	4.9	2.00	640	816.15	2096	39	00	450	116.2	38.98	110.2	34.20
18.	21	6.92	4222	55	5.1	4.00	690	1022.55	2702	41	00	494	131.46	40.44	165.2	41.67
19.	22	7.26	1298	10	5.5	3.20	410	165.93	831	31	00	256	54.50	29.23	177.2	9.21
20.	26	7.35	1125	50	4.2	2.40	400	125.96	720	35	00	248	43.28	34.11	212	5.80
21.	25	7.16	1196	45	1.8	4.80	340	141.65	765	37	00	252	72.9	17.05	240	12.27

													4			
22.	25	7.14	850	50	1.9	5.60	410	76.89	544	27	00	280	80.96	23.39	257	8.10
23.	24	6.95	1070	45	2.5	2.00	440	109.27	884	36	00	302	76.95	26.08	281	34.56
24.	22	7.20	1084	30	1.1	5.60	440	122.76	693	39	00	240	52.90	26.31	100.5	12.70

The physico-chemical parameters were determined for water samples from sampling spots of Kothure Village in the months of May 2008 and September 2008 i.e in the pre-monsoon and post-monsoon periods. The suitability of ground water for drinking, irrigation and domestic uses depends upon its mineral constituents.

The Temperature is a physical parameter which is measured at the site of sampling spot by using thermometer within 5 minutes after sampling. Temperature for all the samples generally varies between 22^0C to 28^0C which is ideal temp.

The Turbidity is one of the physical parameter of water which depends on the scattered particles of dust, micro-organisms etc. The standard limit of turbidance is 5 NTU as per BIS (Bureau of Indian Standards). The value of turbidance varies from 0.7 NTU to 7.9 NTU in pre monsoon. In post monsoon, the value of turbidance varies from 0.7 NTU to 8.1 NTU. The turbidance is classified in 3 groups i.e below 5 NTU, between 5 to 25 NTU and above 25 NTU. During the present investigation all the samples are in the range of 5 to 25 NTU group.

The maximum and minimum values of ph in pre-monsoon are 7.82 and 7.10, which indicates that the ph is of neutral to weakly alkaline nature. The high value of ph is noted for sample no. 24 and low is noted for sample no. 18. In post-monsoon, ph varies between 6.92 to 7.55 which indicates that ph is acidic to weakly alkaline. The high value of ph is in sample no. 15 and low value of ph is in sample no. 18.

The Electrical conductance of water gives an idea about the dissolved ion concentration. Electrical conductance measurement makes it possible to obtain information about the mineralization of ground water. Electrical conductance is an ability of water to conduct electrical cocrrent. Generally it is measured in mhos/cm while in SI unit it is Ws/cm. If the dilution of solution is increased, then the conductance of the solution increased. The electrical conductivity and total dissolved solid (TDS) are related to each other. The total dissolved solid is obtained by multiplying conductivity with 0.64. However, lower EC values can be considered as inactive of lower mineralization of ground water. The permissible limit of electrical conductivity and total dissolved solid is in between 750 mhos/cm to 2250 mhos/cm and 500 mg/lit to 1500 mg/lit resp. The values of EC and TDS are in 250 mhos/cm to 750 mhos/cm at 25 ^{0}C and 500 mg/lit are good for domestic and agricultural purpose. According to WHO (1997), EC of ground water is classified in 3 groups i.e low conductance (below 750 mhos/cm), moderate conductance (between 750 to 2250 mhos/cm) and high conductance (above 2250 mhos/cm). As per data of pre-monsoon sample no. 1,2,11,12,20 has low conductance, sample no. 3,4,5,6,8,10,15,20,21,22,23 is having moderate conductance and sample no. 7,9,13,14,16,17,18,19 have high conductance. In post-monsoon, sample no. 8,9,10 has low conductance, sample no. 1,2,3,4,5,6,7,12,13,15,19,20,21,22,23 and 24 have moderate conductance and sample no. 10,14,17,18 has high conductance values.

The permissible range of Ca and Mg in ground water is 75 to 200 mg/lit and 50 to 150 mg/lit resp. The main source of Ca and Mg in the ground water is dissolution of rocks and leaching from fertilizers. The maximum and minimum values calcium varies between 12.02 to 180.36 mg/lit in pre-monsoon. As per ISI 0500 the calcium content is classified in 3 groups, high calcium (above 200 ppm), medium calcium (between 75-200 ppm) and low calcium (below75 ppm). Sample no. Is medium calcium content. All other samples are low calcium content in case of pre-monsoon results. In case of post-monsoon, values varies between 32.86 to 197.9. Sample no. 7, 13, 14, 16, 17, 18, 22, 23 are medium calcium content whereas sample no. 1, 2, 3, 4, 5, 6, 8, 9, 10, 11, 12, 15, 19, 20 and 24 are low calcium values.

The permissible limit of Chloride content is 250 mg/lit. The maximum and minimum values of chloride in pre-monsoon are 14.84 to 1243.7 resp. As per WHO (1997), chloride content is classified in 3 groups i.e hige (above 600 ppm), moderately high (250-600 ppm) and low (below 250 ppm). In pre-monsoon, sample no. 1, 2, 3, 4, 5, 8, 11, 12, 15, 20, 21, 22, 23,and 24 are low chloride content. Sample no. 6, 9, 10, 13, 14, 17 and 19 are moderately high chloride content and sample no. 7, 16and 18 shows high chloride content. In post-monsoon the maximum and minimum values are 76.89 and 1342.26 resp. Sample no. 1, 2, 3, 4, 5, 6, 8, 9, 11, 15, 19, 20, 21, 22, 23and 24 shows low chloride content while sample no. 10, 12, 13, 14 and 16 shows moderately high values and sample no. 7, 17 and 18 shows high chloride contents.

The hardness means soap does not form leather with water. We observed that sample no. 7 and 18 are medium hard water samples while all other are soft water samples. In post-monsoon, maximum and minimum values of hardness are 116 and650. Sample no. 8, 9, 10, 15, 19, 20, 21, 22, 23 and 24 are soft water samples while sample no. 1, 2, 3, 4, 5, 9, 11, 14, 16, 17, 18 are medium hard water samples and sample no.7 is hard water sample.

The permissible limit of Sodium and Potassium is 100 mg/lit to 150 mg/lit and 10 mg/lit to 15 mg/lit resp.

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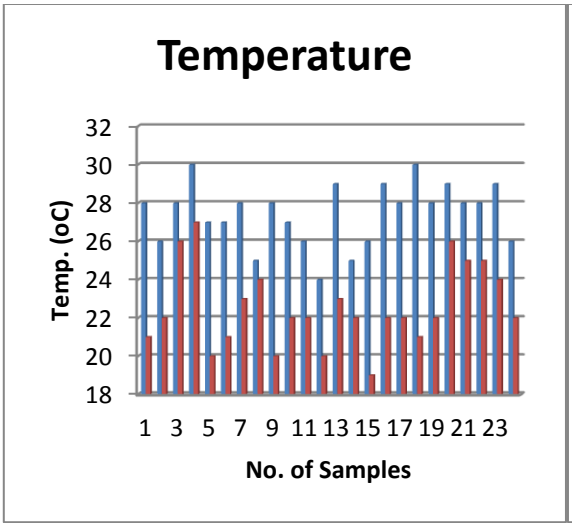
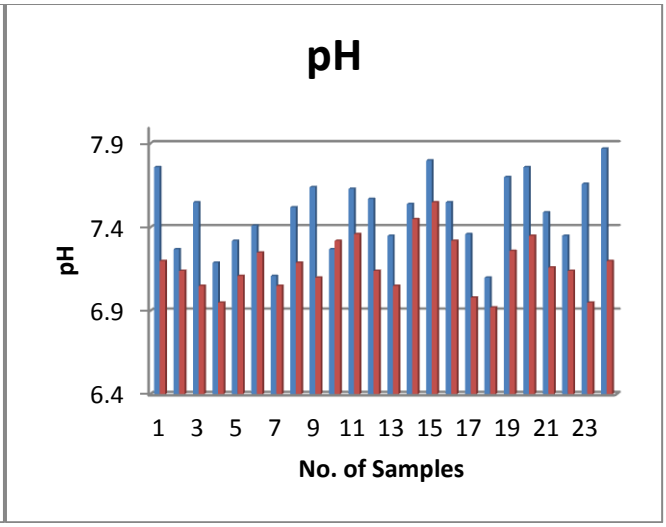
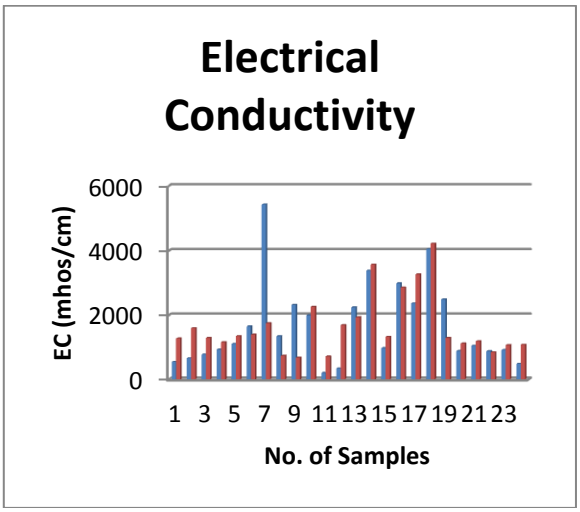
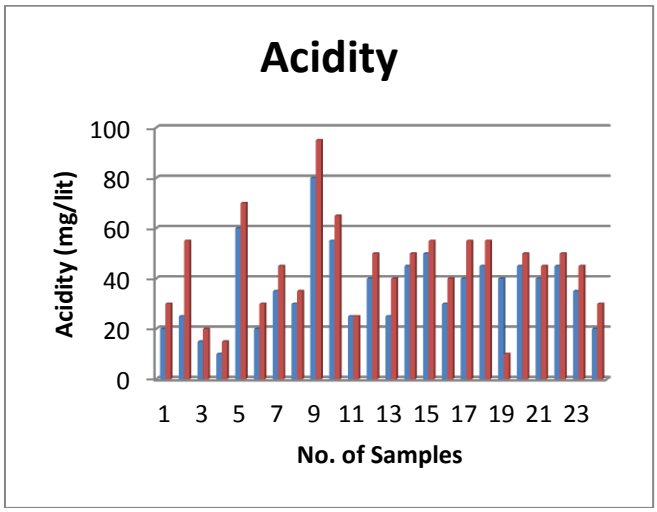
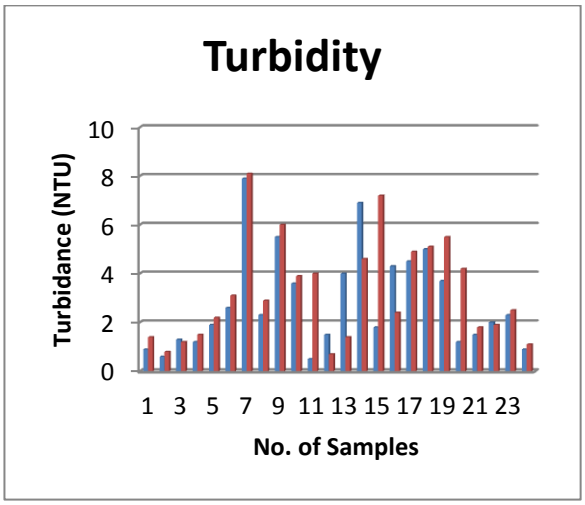
The Results for Pre-monsoon & Post-monsoon periods of present paper are shown graphically as follows –

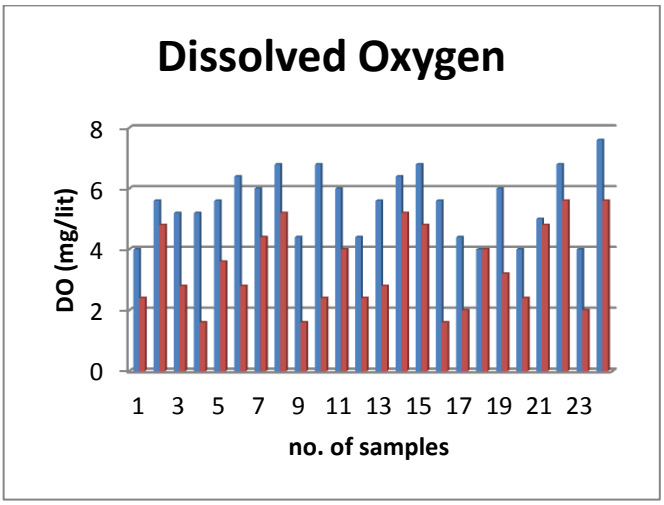












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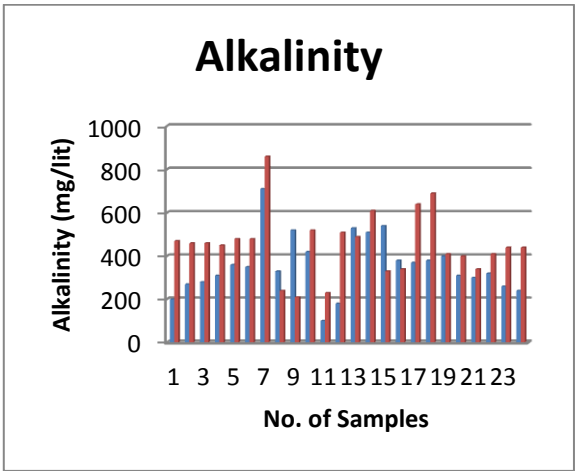

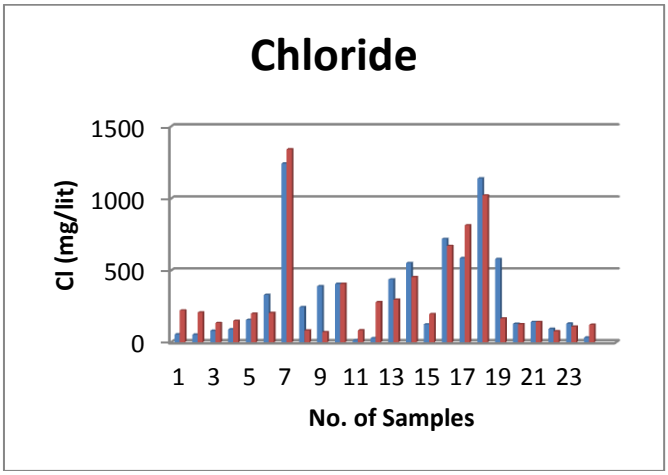

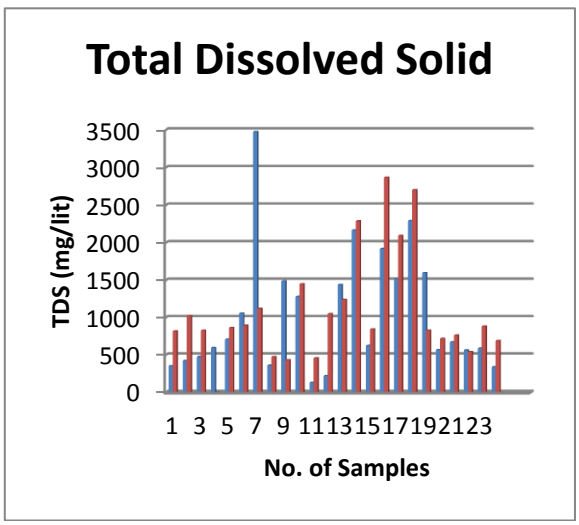

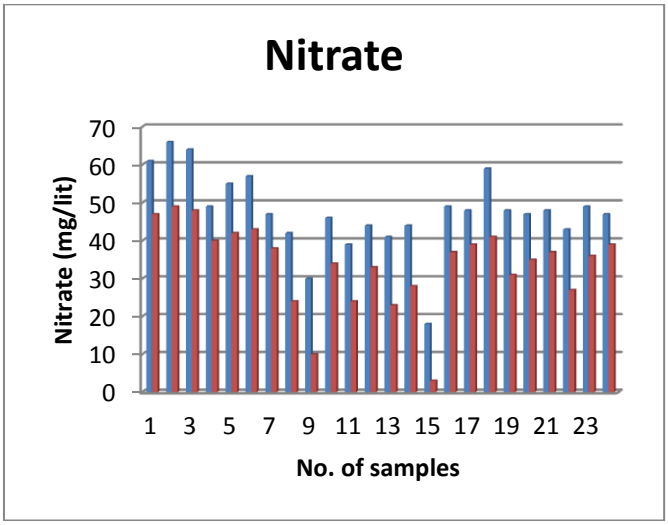

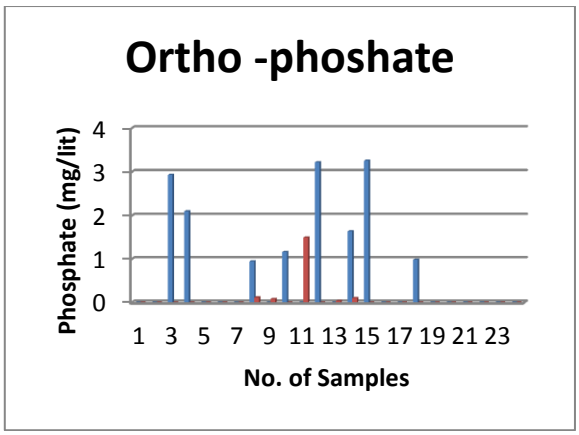

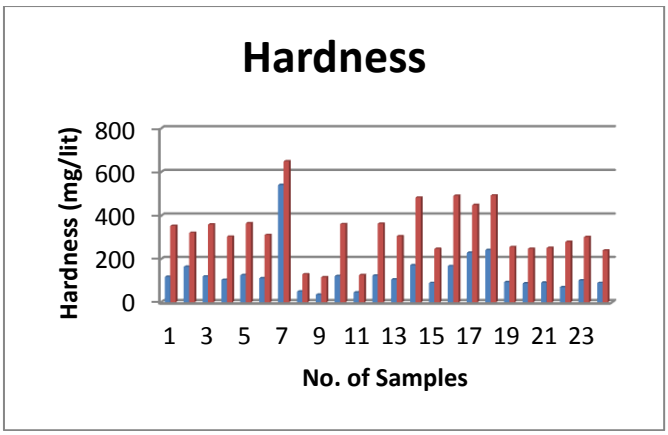

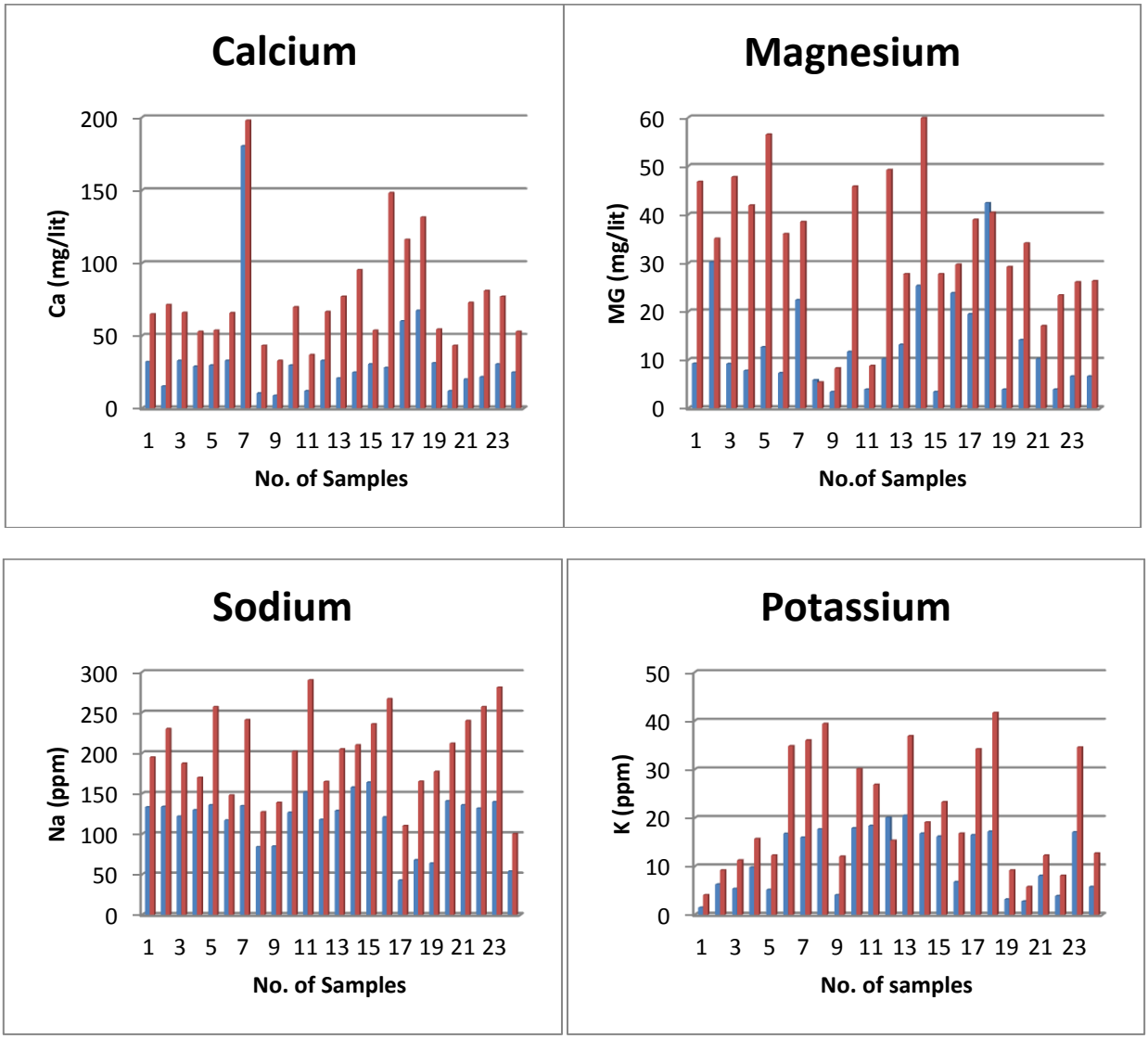

4. CONCLUSION :

To determine the quality of ground water based on the variations in the physic-chemical parameters, a network of 24 sampling stations was established in the area of Kothure Village. The area of Kothure Village was selected for this study because of its richness in the field of agriculture. This village was awarded 'Ideal Village'. There is significant increase in sugar industries around Kothure village. This study was done to check whether there is any impact of sugar industry on quality of ground water in Kothure Village.

The analysis of ground water was done for different samples from various spots in the months of May and September i.e pre-monsoon and post-monsoon. The analysis includes determinations of 16 different parameters like Temperature, ph, Electrical conductivity, Total dissolved solid, Ca, Mg, Na, K, Cl, Hardness, Turbidity, Alkalnity and Acidity etc. The analytical methods include volumetric (Cl, Hardness, Alkalinity, Acidity Ca and Mg), Flame photometric (Na and K), Nephalo turbidity meter (Turbidity), ph-meter (ph) and conductivity meter (Electrical conductivity).

Our study has shown that the parameter values are generally more in pre-monsoon period than post-monsoon. The reason for this is, the water in pre-monsoon period is saturated water while in post-monsoon period it is diluted with free flowing diluted water. Secondly the fertilizers gets diluted with rain water in post-monsoon. So all values are more in pre-monsoon period. We have observed that there are no major deviations in values of the parameters because of increase of sugar industries in this area.

We have observed that there is a lack of phosphate in water of Kothure Village. All the samples are showing very less scale of phosphate in it. Sample no. 7 is having abnormal values of physico-chemical parameters. This well is not in use and water is saturated. The taste of water is also objectionable. So this sample is unsuitable for drinking, irrigation and commercial purpose.

The study of present investigation has led us to conclude that the quality of water samples subjected to study was acceptable from majority of physic-chemical parameters for domestic application as well as commercial

purposes. For domestic purpose, it is recommended to use after practicing suitable disinfection systems. The mineral water is found to be safe for drinking.

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Assessment Of Heavy Metal Concentration In Well Water From Mithsagare Village, Nashik, Maharashtra

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Abstract: *In most countries of the world, ground water and surface water are at a serious risk of pollution due to chemicals used in agricultural activities. Well water is one of the major source of domestic (drinking) water. This study is for the assessment of heavy metal contamination in well water used for domestic purposes. Water samples from the wells are analyzed in the laboratory to asses lead, copper, mercury, chromium, cadmium, iron, zinc, potassium, and phosphate. The results of the analyses were compare with the Standards. The results shows that the conc. of Mg and Mn in well water had higher conc. than maximum permissible limits of standards and the concentration of other heavy metals in well water was at different compliance level with standards. It can be concluded that well water in Mithsagare village (Nashik) is fit for domestic use but that efforts should be made to reduce the Mg and Mn concentration by having control on the anthropogenic factors that lead to such high concentration levels or else soon this source of water may become unfit for domestic use..*

Key Words: *Heavy metals, anthropogenic factors, well water, Contamination, Water quality standards*

1. INTRODUCTION:

Water is the important resource and it is one of the essential commodities of day to day life. [1] Water is necessary for a sustainable economic development of an area. It is a 'Life Sustainer'.[1] Water covers 71 % of the earth's surface. On earth, approximate 96.5% water is found in seas and oceans.1.7% in ground water, 1.7% in ice caps and small fraction in other water bodies.[2] Only one percent of water on the earth comes from sources like rivers, lakes and sustainable aquifers. Increasing world's population is facing water shortages. In Mithsagare village, most of the people depend largely on well water. Rapid growth in population and urbanization, has affected the quality of well water due to over exploitation, and increasing demand for agriculture, domestic and industrial water supply.[3] So preservation and purification of well water is important.

Ground water may be contaminated by different contaminants which have an impact on the health. Due to industrial effluents discharge, and inadequate treatment and solid waste disposal, number of contaminants like heavy metals, nitrates salts enters into the water bodies. Some contaminants occur and move naturally whereas some are due to anthropogenic factors. According to WHO 80% of diseases are arises due to contamination in ground water. In environment the presence of heavy metals has grown because of its large utilization in industries and agricultural activities. Especially the trace metal contamination in ground water shows serious health issues.

Heavy metals are the metallic chemical elements. The term "heavy metals" defined as commonly held for those metals, which have some atomic weight between 63.54 and 200.59 and specific gravity greater than 4. Heavy metals are non-biodegradable and persistent in the environments for long periods, accumulate and not metabolized in other intermediate compounds therefore they are dangerous and shows serous health issues. Although trace amount of some heavy metals are required by living organisms but excess amount of these metals can cause serious toxic problems to life. Occurrence of heavy metals in ground water and surface water is due to natural sources like naturally occurring minerals containing trace elements in the soil zone or to human activities such as mining, fuels, smelting of ores and improper disposal of industrial wastes.

2. Classification of heavy metals:

Heavy metals are classified into four major groups on their health importance.

Sr. No.	Group	Examples
1	Essential	Cu,Zn,CO,Cr,Mn,Fe
2	Non-Essential	Ba, Al ,Li and Zr
3	Less toxic	Sn and As
4	Highly toxic	Hg,Cd, Pb

3. Health Effects and Sources of heavy metals

Metal	Sources of occurrence	General & Health Effects
Calcium Ca (mg/l)	Minerals containing limestone, dolomite	Poor lathering with soap, deterioration of quality of clothes, incrustation in pipes

Magnesium Mg (mg/l)	Minerals containing limestone, dolomite	Poor lathering with soap, deterioration of quality of clothes, with surface laxatives
Fluoride F (mg/l)	Industrial waste, Geological	Brownish discoloration of teeth, bone damage, Skeletal fluorosis
Copper, Cu (mg/l)	Leaching from copper water pipes and tubing, algae treatment, Industrial and mining waste, wood preservatives, Natural deposits	Anemia, Liver and kidney damage, gastrointenstinal irritations, bitter or metallic taste, plumbing fixtures
Iron Fe (mg/l)	Leaching of cast iron pipes in water distribution system	Bitter or metallic taste, brown-green stains, rusty sediment
Sulphate SO_4 (mg/l)	Animal sewage, Septic system, sewage ,By-product of coal mining, industrial waste, Natural deposits or salts	Gastrointestinal irritation, Taste affected, Corrosion
Manganese Mn (mg/l)	Landfills Deposits in rock and soil	Bitter taste ,brownish color
Nitrate NO_3^- (mg/l)	Livestock facilities, Septic systems, Manure ,Fertilizers, Household waste water, Natural Deposits	Blue baby disease in infants,Methemogloinemia
Nitrite NO_2^- (mg/l)	Fertilisers, waste water	Forms Nitrosamines which are carcinogenic
Zinc Zn (mg/l)	Leaching of galvanized pipes and fittings,paints, dyes ,Natural deposits	gastrointestinal irritations, vomiting, dehydration, dizziness, abdominal pain
Chromium Cr(mg/l)	Septic systems, Industrial discharge, Mining sites, Geological.	Skin irritation, skin and nasal ulcers, lung tumors, damage to nervous system and circulatory system,
Sodium Na (mg/l)	Natural component of water	Salty taste to water
Chloride Cl (mg/l)	Fertilizers, Industrial wastes, Minerals, Seawater	High blood pressure, salty taste, corroded pipes, blackening and pitting of stainless steel
HCO3- (mg/l)	Sewage water, waste	Bitter taste, salty taste
Arsenic As (mg/l)	Previously used in pesticides, Improper waste disposal or product storage of glass or electronics, Mining, Rocks	Weight loss, depression, lack of energy, skin and nervous system toxicity
Cadmium Cd (mg/l)	Sewage, Sludge, Fertilizers, Industrial effluents	Highly toxic ,"Itai-Itai disease", Cardiovascular system affected, hypertension
Lead Pb (mg/l)	Paint, diesel fuel combustion, Pipes and solder, Natural deposits	Bio-accumulation, damage to kidneys, abdominal discomfort, Anemia, irritability
Mercury Hg (mg/l)	Fungicides, Mining, Electrical equipment, plant, Natural deposits	Highly toxic, causes "Minamata" disease, mutagenic, renal disturbances

Table 1. Sources of metals and WHO standards

The present study is carried to evaluate the impact of anthropogenic inputs on quality of ground water w.r.t. heavy metals. The concentration of heavy metals above the acceptable levels can result in serious environmental and health problems. This study is helpful to determine heavy metal concentration in well water from selected areas of Mithsagare village. This paper is therefore for analysis of water quality and heavy metal contamination. The results are compared with WHO standards.

4. Materials and Methods:

4.1 Study area

This study was conducted in Mithsagare village located in Sinner Tehsil from District Nashik(Maharashtra).It is nearly about 48 kilometers away from Nashik city. The village is surrounded by industrial area. Most of the people in Mithsagare village depends on agriculture. Well water is major source of domestic water as well as for agricultural activities. To evaluate the quality of well water in Mithsagare village is important for increasing demand for agriculture and domestic purpose.

4.2 Sample collection, preservation and Storage

Six samples for well water were collected from Mithsagare village to assess the contamination w.r.t heavy metals. Water samples were collected in clean, sterilized and transferant polythene containers. The containers were thoroughly rinsed several times with distilled water. After collecting samples all of them were properly sealed and

correctly labeled to avoid confusion. The collected samples were preserved in refrigerator at 1 to 4 ^{0}C until analysis. The samples were tested in laboratory for the presence of heavy metals in well water.

4.3 Data Analysis

The heavy metal concentration in 6 samples of well water from Mithsagare village, were determined in ppm by using Atomic Absorption Spectrophotometer (AAS). Finally, the analyzed data were compared with WHO standards for drinking water quality.

5. Results and Discussion:

The concentration of heavy metals in well water samples from six (6) locations within Mithsagare village was analyzed. The results as shown in table2.

Parameters	W1	W2	W3	W4	W5	W6	WHO Standard
Calcium Ca (mg/l)	56	66	90	65	50	48	75
Magnesium Mg(mg/l)	16.04	18.65	14.25	15.56	20.61	18.65	2
Fluoride F (mg/l)	0.62	0.42	0.52	0.56	0.73	0.4	1.0
Copper Cu (mg/l)	0.08	0.06	0.10	0.12	0.09	0.01	1.0
Iron Fe (mg/l)	0.3	0.04	0.05	0.06	0.0	0.02	0.3
Potassium K(mg/l)	9.2	20	10	8.5	11	9.5	--
Sulphate SO4 (mg/l)	6	5	7	4	30	5	200
Manganese Mn (mg/l)	0.6	0.4	0.2	0.3	0.5	0.3	0.1
Nitrate NO3 (mg/l)	35.14	49	32	43	33	59	45
Nitrite NO (mg/l)	0.050	0.021	0.062	0.021	0.042	0.013	0.2
Zinc Zn (mg/l)	0	0.1	0	0.2	0	0	5
Phosphate (mg/l)	0.35	0.75	0.3	0.42	0.56	0.47	---
Chromium Cr(mg/l)	0.02	0.01	0	0.02	0.01	0.01	0.05
Sodium Na (mg/l)	115.5	122	152	130	68	149	180
Chloride Cl (mg/l)	102	140.5	122	139	115	80.2	250
HCO3- (mg/l)	42	35	30	45	40	32	100

Table 2. Results of laboratory analysis of well water samples in Mithsagare village.

Magnesium is one of the essential element for proper growth and development of plants. It is constituent in chlorophyll pigment which is responsible for photosynthesis. The high content of Magnesium and Calcium in water results to hardness of water. Poor lathering and deterioration of clothes occurs due to hard water. The analyzed data were compared with WHO standards. The amount of magnesium in well water samples as obtained from laboratory analysis indicates the values higher than permissible limit of 2.0 mg/l required for drinking water quality as shown in table 2.

Iron is naturally occurring metal in nature in the form of ore. Iron enters into the water bodies through leaching of cast iron pipes in distribution systems or naturally. Iron is essential element for dietary requirement for most of organisms. Its defects leads anemia. Excess concentration of iron causes gastrointestinal irritation and increases the growth of iron bacteria that affects the water taste[4]. Iron content in water gives bitter or metallic taste to water. It can also result in gene mutation. The iron concentration of the samples is in between 0.00-0.30 mg/l which is within the permissible limit of WHO standard.

The Manganese is one of the common essential trace element and toxic. Manganese gives a bitter taste to water. It promotes the growth of algae that form a slimy coating in pipes. The values obtained far exceeds the permissible limit of WHO standards.

Zinc is essential trace metal. It enters into water from industrial waste water, galvanic industries etc [4] The high concentration of Zn gives metallic taste to water. The values obtained are below the limit of 5 mg/l compared with WHO.

Trace amount of chromium compound are present in water. It discharged into ground water through refinery industries and alloy industries, or industrial effluents. Excess concentration causes skin irritation, gastrointestinal effects, damage to the nervous system, circulatory system. The analyzed data indicates the values fall within the permissible limits of 0.05 mg/l. shown in table 2.

Copper is one of the heavy metal which enters into ground water due to industrial wastage containing copper, agriculture pesticides and released into drinking water through corrosion of copper pipes. It is essential element but excess concentration in drinking water causes kidney and liver damage in people. Wilson's disease is example of copper toxicity [4]. The values compared with standards are within limit as shown in table 2.

When the chloride content in water is 250 mg/l, then it is detected by salty taste. The chloride content in the water samples are in between 80.2 mg/l to 140.5 mg/l. High concentration in water is due to industrial waste discharges, and use of fertilizers.

Nitrate is major plant nutrient. It enters into water naturally or through sludge, sewage, fertilizers. Higher concentration of nitrate in water causes disease Methenoglobinemia or blue baby disease in infants. Four analyzed samples are within desirable limit of WHO standard but two samples exceeds the limit more than 45 mg/l. It may be due to the contamination of water by human activities.

The Sodium (Na) content in collected water samples varies from 68 mg/l to 149 mg/l. Higher concentration of sodium in water is unsuitable for drinking purpose.[1] The Potassium (K) content in water samples varies from 20mg/l to 8.5 mg/l. Results of the analysis of the heavy metals in water samples of Mithsagare well are given below

6. CONCLUSION:

The assessment of well water quality is necessary because large number of people consume water from wells in Mithsagare village (Nashik). The survey shows that most of the wells are present in agricultural areas. Due to use of fertilizers and industrial waste discharges, sewage, contamination of well water w.r.t heavy metals may occur.
The result of the analysis shows that the concentration of elements like iron, copper, potassium,zinc,sodium in well water from Mithsagare village falls within permissible limit of WHO standards. While the concentration of Manganese and Magnesium far exceeds the limit which is unsatisfactory when compared with WHO standard. The concentration of Nitrate in four water samples are within limit but two exceeds the limit. It can be concluded that well water from Mithsagare village is fit for human consumption and suitable for other domestic purposes. But the efforts should be taken to reduce the concentration of manganese and magnesium in well water by controlling anthropogenic factors. Frequent monitoring of well water for contamination by heavy metals is necessary to avoid the human health risk.

7. RECOMMENDATIONS:

- It is recommended that the precautionary measure should be taken immediately to avoid the harmful effects by high concentration of heavy metals on human health.
- To avoid future consequence the frequent monitoring of well water is required by controlling anthropogenic factors.
- Before using well water for drinking purpose the water treatment to reduce Manganese concentration like Ion exchange, Chlorination, Oxidizing filter etc. should be done.

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