

# Anti-cancer assay on various cell lines of Caryophyllales order

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**Abstract:** Medicinal plants are considered as a rich resources of ingredients which can be used in drug development and drug designing. Medicinal plants are only solutions to cure a number of health related problems and diseases. Several species of the Caryophyllales order are widely used by many ethnic communities as traditional medicine throughout the world. The highest number of plants of this family are used in Chinese traditional medicine. The Caryophyllales is a diverse order that includes trees, shrubs, lianas, mangroves, stem or leaf succulents and insectivores plants. These plants has many pharmacological activity like antimicrobial, antiviral, antioxidant, anticancer, anti-inflammatory and antiplasmodial. This review paper reveals the anti-cancer activity present in the order Caryophyllales.

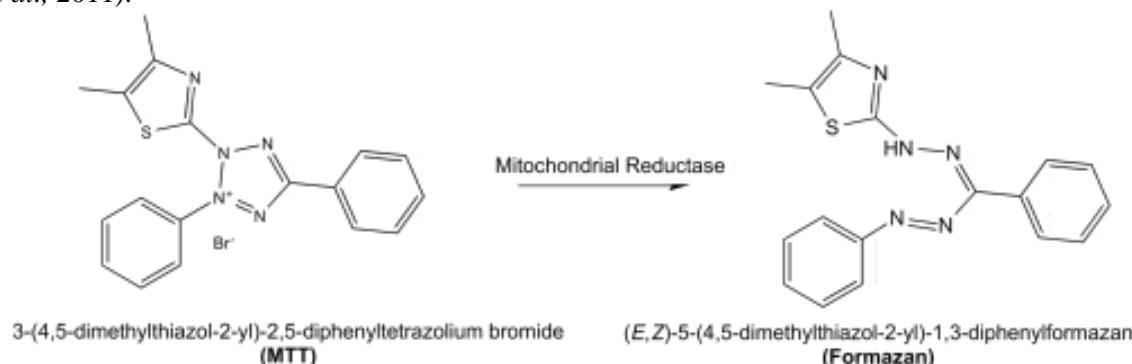
**Key Words:** Caryophyllales, antioxidant, anticancer, anti-inflammatory, antiplasmodial.

## 1. INTRODUCTION:

Cancer is not just one disease, but a group of more than hundred diseases in which a group of cells become abnormal and the division of cells become uncontrollable (Kumari *et al.*, 2017). Cancer cells can spread through the blood circulation or lymph system in the other parts of the body. The swelling occurs in the part of body due to abnormal growth of cells or tissues is called tumor. On the basis of origin of the tumor and type of tumor cells, cancer can be classified as below categories :- Carcinoma, Sarcoma, Leukemia, Lymphoma, Myeloma, Blastoma, Central nervous system cancers. Caryophyllales are a highly diverse and large order of flowering plants that includes the cacti, carnations, amaranths, ice plants, beets, and many carnivorous plants(Pucker *et al.*, 2020). This family is popularly known as the pink family or carnation family(Chandra and Rawat., 2015). Many members are succulent, having fleshy stems or leaves(White *et al.*, 2017). The members of Caryophyllales include about 6% of dicot species. Presently, the Caryophyllales contains 39 families, 749 genera and 12,500 species ( Hernández-Ledesma *et al.*,2015). Caryophyllales includes plants ranging from garden subjects and vegetables to weird succulent plants that resemble stones. The garden plants include carnations, pinks, four-o'clocks, amaranths, portulacas, and Madeira vines. Vegetables in the order include beets, spinach, and Swiss chard. Aizoaceae includes ice plants, sea figs (also called beach apples), and living stones (lithops). Succulents plants in Cactaceae and Aizoaceae are commonly collected and used in rock gardens.

## 2. MTT Assay:

MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) is a tetrazolium dye which is yellow in colour. The MTT assay is a colorimetric assay which is mainly used for evaluating or estimating cell metabolic activity (Vajrabhaya and Korsuwannawong., 2018). Furthermore tetrazolium dye assays can be used to measure cytotoxicity (loss of viable cells) or cytostatic activity (shift from proliferation to quiescence) of potential medicinal agents and toxic materials (Stone *et al.*,2009). MTT assays are usually done in the dark since the MTT reagent is sensitive to light. It is mainly based on the ability of dependent cellular oxidoreductase enzymes NADPH (nicotinamide adenine dinucleotide phosphate) that convert tetrazolium dye MTT into insoluble formazan compound, which has a purple color (Van Meerloo *et al.*, 2011).



### 3. SRB Assay:

Sulforhodamine B (SRB) is also known as cell cytotoxicity assay. It is one of the most widely used methods to detect cell viability or drug cytotoxicity. This assay depends on the ability of SRB to bind cellular protein components and measure the total biomass (Duong et al., 2013(29)). SRB is a bright- pink amino xanthene dye which have electrostatic complex with basic amino acid residues of proteins in slightly acidic conditions but it can detach under some simple basic conditions (Mauludin et al., 2009)

**Table : List of plants belonging order Caryophyllales having anticancer properties.**

Sr. No	Plant Name	Family	Common Name	Parts Used	Extract Used	Cancer Cell Line used	Assay used	References
01	<i>Achyranthes aspera L</i>	Amaranthaceae	Chaff-flower, prickly Chaff flower, Devil's horsewhip	Root	Ethanol extract	liver (Hep-2) & colon (HT-29) cell lines.	SRB assay	Singh et al., 2017
02	<i>Aerva javanica</i>	Amaranthaceae	Kapok bush, pillow-weed, desert cotton	Leaves	Methanol, Chloroform, Petroleum ether, acetone extract	Human breast carcinoma cells (MCF-7) and human prostate cancer cells (PC3)	MTT assay	Shehri and Moustafa., 2019
03	<i>Aerva lanata L.</i>	Amaranthaceae	Mountain knotgrass	Flowering aerial part	Ethanol extract	Hela (Cervix), A549 (Lung), Caco (Colon), PC-3(Prostate), THP-1 (Leukaemia) cell lines	SRB assay	Bhanot et al., 2013
04	<i>Alternanthera sessilis</i>	Amaranthaceae	Garundi	Aerial, stem and leaves	Ethanol extract	HT-29 cells and 3T3 cells	MTT Assay	Gothai et al., 2018
05	<i>Amaranthus spinosus Linn</i>	Amaranthaceae	Prickly Amaranth, Spiny amaranth, Thorny amaranth	Leaves	Petroleum Ether , Ethyl Acetate, Ethanol Extract	Human cervical cancer cell line (HeLa).	MTT assay	Saravanan., 2016
06	<i>Amaranthus viridis L.</i>	Amaranthaceae	Green amaranth	Whole plant	Petroleum Ether, Ethyl Ether, Ethyl Acetate, N-Butanol, Methanolic Extract	HT-29 and HpeG 2 cells	MTT based assay	Jin et al., 2013

07	<i>Basella alba</i>	Basellaceae	Malabar spinach, vine spinach, Ceylon spinach	Leaves	Aqueous extract	Ehrlich's Ascites Carcinoma (EAC)	-	Islam <i>et al.</i> , 2018
08	<i>Boerhaavia diffusa</i> Linn	Nyctaginaceae	Punarnava	Whole plant	Ethanol extract	SiHa cell line	MTT Assay	Venkatajohi., 2017
09	<i>Boerhaavia erecta</i>	Nyctaginaceae	Erect spiderling, Erect boerhavia	Whole plant	Methanolic extract	Mouse fibroblastic cell lines (L929), Human brain glioblastoma cell lines (U87)	MTT Assay	Shareef <i>et.al.</i> , 2017
10	<i>Bougainvillea glabra</i>	Nyctaginaceae	lesser bougainvillea, paper flower	Leaves	Petroleum ether extract	HeLa cancer cell line	MTT assay	Joshny <i>et al.</i> , 2012
11	<i>Bougainvillea peruviana</i>	Nyctaginaceae	Peru Buganvilla	Leaves	Ethanol extract	HeLa cancer cell line	MTT Assay	Medpilwar <i>et al.</i> , 2019
12	<i>Opuntia ficus-indica</i>	Cactaceae	Indian fig opuntia, Barbary Fig, Cactus pear	Prickly pear fruits	Ethanol, Ethyl acetate extract	Liver(HepG2), Colorectal adenocarcinoma (Caco-2), Breast cell line (MCF-7)	-	Beltagi <i>et al.</i> , 2019
13	<i>Opuntia polyacantha</i>	Cactaceae	plains prickly pear, hair spine cactus, prickly pear	Aerial parts	Methanol (80%), Chloroform Extract	MCF-7 and WRL-68 cell lines	MTT assay	Abdulazee m <i>et al.</i> , 2018
14	<i>Opuntia stricta</i>	Cactaceae	Erect prickly pear	Flowers	Ethanol extract	HepG2 cell line.	MTT assay	Prabhakaran <i>et al.</i> , 2017
15	<i>Plumbago zeylanica</i> Linn.	Plumbaginaceae	Ceylon leadwort, doctor bush, wild leadwort	Roots	Alcoholic, aqueous extracts, Hydro-alcoholic extracts extract	HCT-15 cells,	-	Sharma <i>et al.</i> , 2015

16	<i>Plumbago auriculata</i> Lam.	Plumbaginaceae	Blue plumbago, Cape plumbago, Cape leadwort	Whole plant	Methanolic extract	A549 cells, PA1 cells	MTT Assay	Lakshmanan <i>et al.</i> , 2016
17	<i>Polygonum bistorta</i> L.	Polygonaceae	Snake root, Snake weed, Easter-ledges.	Rhizome	Methanol, Aqueous, Ethanolic extract	human hepatocellular carcinoma cell line (HCCLM3)	-	Intisar <i>et al.</i> , 2013
18	<i>Reaumuria vermiculata</i>	Tamaricaceae	hong sha shu	Shoot part	Hexane, Dichloromethanol, Methanol, Aqueous extract	A-549 lung carcinoma cells lines	-	Karker <i>et al.</i> , 2016
19	<i>Rumex nervosus</i>	Polygonaceae	Crested Dock, Greek Dock	Leaves	Chloroform extract	MCF-7 and MDA-MB-231 cells	-	Quradha <i>et al.</i> , 2019
20	<i>Rumex vesicarius</i>	Polygonaceae	Ruby dock, Bladder dock	Whole plant	Methanolic extract	HepG2 cells	MTT assay	Londonkar <i>et al.</i> , 2015
21	<i>Saponaria vaccaria</i>	Caryophyllaceae	Cowherb, Cowcuckle, Cow Basil, Cow Soapwort, Prairie Carnation.	Seed	Methanolic extract	WiDr (colon), MDA-MB-231 (breast), NCI-417 (lung), PC-3 (prostate) , BJ (CRL-2522) cell line.	MTT assay	Balsevich <i>et al.</i> , 2012
22	<i>Sesuvium portulacastrum</i>	Aizoaceae	Shoreline Purslane, Sea Purslane,	Whole plant	Ethanol, Methanol, Acetone, Hexane, Diethyl ether extract	MCF – 7	MTT Assay	Chintalapani <i>et al.</i> , 2018
23	<i>Suaeda monoica</i>	Amaranthaceae	South-Indian Seepweed	Whole plant	Ethanol, Methanol, Acetone, and Diethyl ether extract	MDAMB-231 cells	SRB assay	Sudarshan <i>et al.</i> , 2019

24	<i>Tamarix nilotica</i> (Ehrenb.)	Tamaric acae	Nile tamarisk	Flowers	Chloroform, Petroleum ether, Ethyl acetate, butyl alcohol extract	Liver (Huh-7) and lung (A-549) cell lines	SRB assay	Bakr <i>et al.</i> , 2013
25	<i>Tamarix aphylla</i> L.	Tamaric acae	Athel tamarisk , Athel tree, Athel pine, saltcedar.	Leaves	Methanolic , ethanolic extract	MCF-7 cancer cells	-	Sobeai <i>et al.</i> , 2018

#### 4. CONCLUSION:

The gradually rising trend of applying bioactive extracts and pure components of plant origin to treat and prevent cancer stems mainly from the almost inescapable severe side effects involving the use of chemical drugs and their frequently low effectiveness. The ethnopharmacological studies of this family indicate that plants of the family possess antibacterial, antiviral, anticancer, antifungal, antioxidant, and anti-inflammatory properties. The experimental works disclosed in this review paper, the value of plants of the Caryophyllales order as potential sources for preventive and curative anticancer drugs. Based on available literature as presented in our manuscript, studies conducted using various cancer cell lines have provided impressive evidence of anticancer activities. MTT assay and SRB assay are mainly used to find anticancer activity present in the plants. The plants of Caryophyllales order having excellent anticancer potential.

#### REFERENCES

1. Kumari, R., Kaur, J., & Kajal, M. (2017). A Review on Quality of Life in Cancer Patients: An Indian Scenario. *Int J Cur Res Rev/ Vol*, 9(15), 45.
2. Pucker, B., Feng, T., & Brockington, S. (2020). Next generation sequencing to investigate genomic diversity in Caryophyllales-Pharnaceum exiguum.
3. Chandra, S., & Rawat, D. S. (2015). Medicinal plants of the family Caryophyllaceae: a review of ethno-medicinal uses and pharmacological properties. *Integrative medicine research*, 4(3), 123-131.
4. White, P. J., Bowen, H. C., Broadley, M. R., El-Serehy, H. A., Neugebauer, K., Taylor, A., ... & Wright, G. (2017). Evolutionary origins of abnormally large shoot sodium accumulation in nonsaline environments within the Caryophyllales. *New Phytologist*, 214(1), 284-293.
5. Hernández-Ledesma, P., Berendsohn, W. G., Borsch, T., Von Mering, S., Akhani, H., Arias, S., ... & Fuentes-Bazán, S. (2015). A taxonomic backbone for the global synthesis of species diversity in the angiosperm order Caryophyllales. *Willdenowia*, 45(3), 281-383.
6. Vajrabhaya, L. O., & Korsuwannawong, S. (2018). Cytotoxicity evaluation of a Thai herb using tetrazolium (MTT) and sulforhodamine B (SRB) assays. *Journal of Analytical Science and Technology*, 9(1), 15.
7. Stone, V., Johnston, H., & Schins, R. P. (2009). Development of in vitro systems for nanotoxicology: methodological considerations. *Critical reviews in toxicology*, 39(7), 613-626.
8. Van Meerloo, J., Kaspers, G. J., & Cloos, J. (2011). Cell sensitivity assays: the MTT assay. In *Cancer cell culture* (pp. 237-245). Humana Press.
9. Duong, H. H. P., & Yung, L. Y. L. (2013). Synergistic co-delivery of doxorubicin and paclitaxel using multi-functional micelles for cancer treatment. *International journal of pharmaceutics*, 454(1), 486-495.
10. Mauludin, R., Müller, R. H., & Keck, C. M. (2009). Development of an oral rutin nanocrystal formulation. *International journal of pharmaceutics*, 370(1-2), 202-209.
11. Singh, S., Verma, S. K., & Singh, S. K. (2017). In-vitro anticancer activity of Achyranthes aspera root extract against different human cancer cell lines.
12. Al-Shehri, M., & Moustafa, M. (2019). Anticancer, Antibacterial, and Phytochemicals Derived From Extract of *Aerva javanica* (Burm. f.) Juss. ex Schult. Grown Naturally in Saudi Arabia. *Tropical Conservation Science*, 12, 1940082919864262.
13. Bhanot, A., Sharma, R., Singh, S., Noolvi, M. N., & Singh, S. (2013). In vitro anti cancer activity of ethanol extract fractions of *Aerva lanata* L. *Pak. J. Biol. Sci*, 16, 1612-1617.

14. Gothai, S., Muniandy, K., Esa, N. M., Subbiah, S. K., & Arulselvan, P. (2018). Anticancer potential of Alternanthera sessilis extract on HT-29 human colon cancer cells. *Asian Pacific Journal of Tropical Biomedicine*, 8(8), 394.
15. Saravanan, R. (2016). "Evaluation of In-Vitro and In-Vivo Anticancer Activity of Leaf Extracts of *Amaranthus Spinosus Linn.*" (Doctoral dissertation, College of Pharmacy Madras Medical College, Chennai).
16. Jin, Y. S., Xuan, Y., Chen, M., Chen, J., Jin, Y., Piao, J., & Tao, J. (2013). Antioxidant, Antiinflammatory and Anticancer Activities of Amaranthus viridis L. Extracts. *Asian Journal of Chemistry*, 25(16).
17. Islam, M., Rahi, M., Jahangir, C. A., Rahman, M. H., Jerin, I., Amin, R., ... & Reza, M. A. (2018). "In Vivo Anticancer Activity of *Basella alba* Leaf and Seed Extracts against Ehrlich's Ascites Carcinoma (EAC) Cell Line." *Evidence-Based Complementary and Alternative Medicine*, 2018.
18. Venkatajothi, R. (2017). In-vitro anticancer activity of Boerhaavia diffusa Linn. *Int. J Curr. Res. Biol. Med*, 2, 20-24
19. Shareef, M. I., Gopinath, S. M., Gupta, A., & Gupta, S. (2017). Antioxidant and anticancer study of Boerhavia erecta. *Int. J. Curr. Microbiol. Appl. Sci*, 6(9), 879-885.
20. Joshny, J., Devi, R. D., & Hari, V. B. (2012). Anti-cancer and anti-microbial activity of hydro alcoholic extract of bougainvillea glabra. *Int J Curr Pharm Rev Res*, 3, 79-85.
21. Medpilwar, M., Maru, D., Vernekar, M., & Harmalkar, M. (2019). Evaluation of Anti-Microbial and Anti-Cancer Activity of Ethanolic Extracts of Bougainvillea shubhra and Bougainvillea peruviana. *Acta Scientific Nutritional Health*, 4(1).
22. El-Beltagi, H. S., Mohamed, H. I., Elmelegy, A. A., Eldesoky, S. E., & Safwat, G. (2019). Phytochemical screening, antimicrobial, antioxidant, anticancer activities and nutritional values of cactus (*Opuntia Ficus Indicia*) pulp and peel. *Fresenius Environmental Bulletin*, 28, 1534-1551.
23. Abdulazeem, L., Al-Alaq, F. T., Alrubaei, H. A., Al-Mawlah, Y. H., & Alwan, W. K. (2018). Anti-cancer activity of *Opuntia polyacantha* alkaloid extract on human breast cancer cell line. *Journal of Pharmaceutical Sciences and Research*, 10(7), 1753-1754.
24. D. Prabhakaran, M. M. Senthamilselvi and A. Rajeshkanna (2017) "Anticancer activity of *Opuntia stricta* (Flowers) against human liver cancer (HEPG2) cell line" *Journal of Pharmacy Research* , 11(7),793-797
25. Sharma, R., Naik, S., Saroch, V., & Chasoo, G. (2015). A comparative anticancer activity of *Plumbago zeylanica* collected from northern and southern parts of India. *JWorld Journal of Pharmaceutical Research*, 4(7), 1145-51.
26. Lakshmanan, G., Bupesh, G., Vignesh, A., Sathyaseelan, A., & Murugesan, K. (2016). Micropropagation and anticancer activity of methanolic extract of *Plumbago auriculata* Lam. *International Journal of Advanced Biotechnology and Research*, 4, 2001-2011.
27. Intisar, A., Zhang, L., Luo, H., Kiazolu, J. B., Zhang, R., & Zhang, W. (2013). Anticancer constituents and cytotoxic activity of methanol-water extract of Polygonum bistorta L. *African Journal of Traditional, Complementary and Alternative Medicines*, 10(1), 53-59.
28. Karker, M., Falleh, H., Msada, K., Smaoui, A., Abdelly, C., Legault, J., & Ksouri, R. (2016). Antioxidant, anti-inflammatory and anticancer activities of the medicinal halophyte *Reaumuria vermiculata*. *EXCLI journal*, 15, 297.
29. Quradha, M. M., Khan, R., Rehman, M. U., & Abohajeb, A. (2019). Chemical composition and in vitro anticancer, antimicrobial and antioxidant activities of essential oil and methanol extract from Rumex nervosus. *Natural product research*, 33(17), 2554-2559
30. Londonkar, R. L., Nayaka, H. B., & CB, S. K. (2015). Cytotoxicity and hepatoprotective attributes of methanolic extract of Rumex vesicarius L. *Biological research*, 48(1), 19.
31. Balsevich, J. J., Ramirez-Erosa, I., Hickie, R. A., Dunlop, D. M., Bishop, G. G., & Deibert, L. K. (2012). Antiproliferative activity of *Saponaria vaccaria* constituents and related compounds. *Fitoterapia*, 83(1), 170-181.
32. Chintalapani, S. A. T. H. V. I. K. A., Swathi, M. S., & Mangamoori, L. N. (2018). Phytochemical screening and in vitro antioxidant activity of whole plant extracts of *Sesuvium portulacastrum* L. *Asian J Pharm Clin Res*, 11(1), 1-6.
33. Sudarshan, s. M., chintalapani, s., & Narasu, m. L. (2019). Phytochemical analysis and determination of antibacterial and anticancer activities of sueda monoica. *Phytochemical analysis*, 12(12).
34. Bakr, R. O., El Raey, M. A. E. A., & Ashour, R. S. (2013). Phenolic content, radical scavenging activity and cytotoxicity of *Tamarix nilotica* (Ehrenb.) bunge growing in Egypt. *Journal of Pharmacognosy and Phytotherapy*, 5(3), 47-52.
35. Al Sobeai, S. M. (2018). Anticancer, Cytotoxic Effect of *Tamarix aphylla* , and Antibacterial Screening Efficiency Against Multidrug-Resistant Human Pathogens. *Asian J Pharm Clin Res*, 11(11), 241-246.