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Original Article

Marigold Extracts and Their Cytotoxic Effects on Cancer Cells: A Review

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ABSTRACT

As a result of its ability to evade cell death and multiply uncontrolled, cancer remains a top killer globally. Conventional therapies such as chemotherapy, radiation, and surgery often result in severe side effects, drug resistance, and limited efficacy. Therefore, there is an ongoing search for safer, natural alternatives with potent anticancer activity. The genus Tagetes, particularly Tagetes erecta (marigold), belonging to the Asteraceae family, has shown promising therapeutic potential. Antioxidant, anti-inflammatory, and anticancer effects are attributed, in part, to the abundance of bioactive chemicals found. These substances include carotenoids (especially lutein and zeaxanthin), thiophenes, and triterpenoids. Essential oils and marigold extracts have been shown operative for cancer cells, including leukaemia, colon, and lung cancer, in both laboratory and animal experiments. These extracts induce apoptosis, arrest the cell cycle, and enhance antioxidant defenses. Toxicological studies indicate a high safety margin, with no major adverse effects observed in acute, subchronic, or chronic toxicity evaluations. This positions Tagetes erecta as a promising candidate for the development of novel anticancer therapies with minimal side effects.

Keywords: Cancer, Apoptosis, Tagetes erecta, Marigold, Asteraceae, Anticancer activity, Natural alternatives, Flavonoids, Carotenoids, Lutein, Zeaxanthin, Thiophenes, Antioxidant, In vitro studies, In vivo studies, Essential oils, Lung cancer, Colon cancer

INTRODUCTION

Both Singh et al. (2016) and Barhoi et al. (2021) agree that cancer is a main health concern. [1] Its distinguishing characteristic is the rapid proliferation of cells that evades cell cycle checkpoints. Even though cancer biology is advancing at a rapid pace, the cancer incidence and mortality rate are still going up. [3] These diagnostic methods, unfortunately, failed to yield the desired outcomes. Further complications associated with these treatments include cancer recurrence, non-target organ harm, and drug resistance (Choudhari et al., 2020). In order to fight this deadly disease, scientists are continuously seeking out novel anticancer medicines that show promise, ideally with better efficacy and less side effects [7]. To skilfully evade cell death by apoptosis, cancer cells accumulate a number of genetic and epigenetic changes (Klein, 2004). The development of anticancer chemotherapeutics may thus depend on substances that may induce cell death in cancer cells (Lee, 1999). [8] Several cancer treatments derived from plants account for about 75% of the total (Craig, 1999). [9] Surprisingly, essential oils, which are widely distributed in nature, have never been used for their anticancer properties while being widely used in aromatherapy, perfumery, food and flavoring, and other fields. It is generally known that several essential oils or their components have strong antibacterial and antifungal properties. [10] Asteraceae family includes the genus Tagetes, which has 56 species, including 29 perennials and 27 annuals. Around the world, Tagetes sp. are cultivated as multipurpose plants, with the most popular species being T. minuta, T. erecta, T. patula, and T. tenuifolia (Vasudevan et al., 1997). [11] Folk medicine has utilized Tagetes sp. to treat stomach and intestinal disorders. Carotenoids, which are utilized as food coloring and feed additives, are among the highly intriguing biologically active chemicals that come from this species.and having antiaging and anticancer benefits (Block et al., 1992), flavonoids with pharmacological qualities (Tereschuk et al., 1997), and essential oils with antibacterial and insecticidal qualities (Piscaglia et al., 1996). T. minuta L. volatile oils have a suppressive biological action and are

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utilized as food flavorings and perfumes (Chamorro et al., 2008), as well as antibacterial agents (Senatore et al., 2004). in opposition to certain diseases and insects (Vasudevan et al., 1997). The Lamiaceae family includes the genus Ocimum. [12] When it comes to cancer-related deaths, pancreatic cancer is second to none in the world. in [13] Chronic pancreatitis, obesity, heavy alcohol use, cigarette smoking, and a diet rich in red meat are some of the risk factors for pancreatic cancer. [14] Because there are no symptoms of the disease, pancreatic cancer is frequently discovered in its advanced stages. [15] Surgery is still the most effective treatment, although as previously said, the patient's chances of survival are low. [16] The next step is radiation and chemotherapy. [17] The herb is used to treat the common cold, bronchitis, and the common cold. The leaves' juice is used to make sarache. [18-19] The roots' extract is used as a laxative. Traditionally, Tagetes erecta and Tagetes patula leaf juice has been utilized as an antimalarial and antipyretic. Tagetes minuta has a potent larvicidal activity and has long been used to ward off mosquitoes. [20] Tagetes patula juice is used to treat cuts and wounds because it contains iodine. Its floral juice is used as a carminative. In addition to being utilized in food, Tagetes lucida is also used to scent bath water with its leaves and flower heads. [21] Traditional Mexican teas made from Tagetes lucida and Tagetes filifolia shoots are popular beverages and natural cures for indigestion and colic. In the perfumery industry, Tagetes minuta oil is well-liked due to its powerful and piercing scent. Terpenoids, thiophenes, flavonoids, carotenoids, and phenolic chemicals are found in Tagetes species [22] The herbaceous genus Tagetes includes over fifty species of annual and perennial plants belonging to the Compositae and Asteraceae families. Genda Phool (Marigold) is the local name for Tagetes erecta L. Indian marigolds are a traditional spice. [23] The A foundational ingredient in the majority of Indian curries, marigold is a flavor-enhancing spice. Using marigolds in curry dishes has a history that spans over five thousand years. [24] The tall, branching plant originally hails from Mexico and other warmer regions of the United States but has since been eradicated from the subtropics and tropics, including Bangladesh and India. [25]

OBJECTIVES:

1.The primary objective of anticancer activity research involving marigold (Tagetes erecta) is to explore its potential as a natural source of therapeutic agents for cancer treatment. [26]

2.Identifying Bioactive Compounds: Isolating and characterizing the specific compounds6 responsible for marigold's anticancer activity. [27]

Taxonomical classification [28]

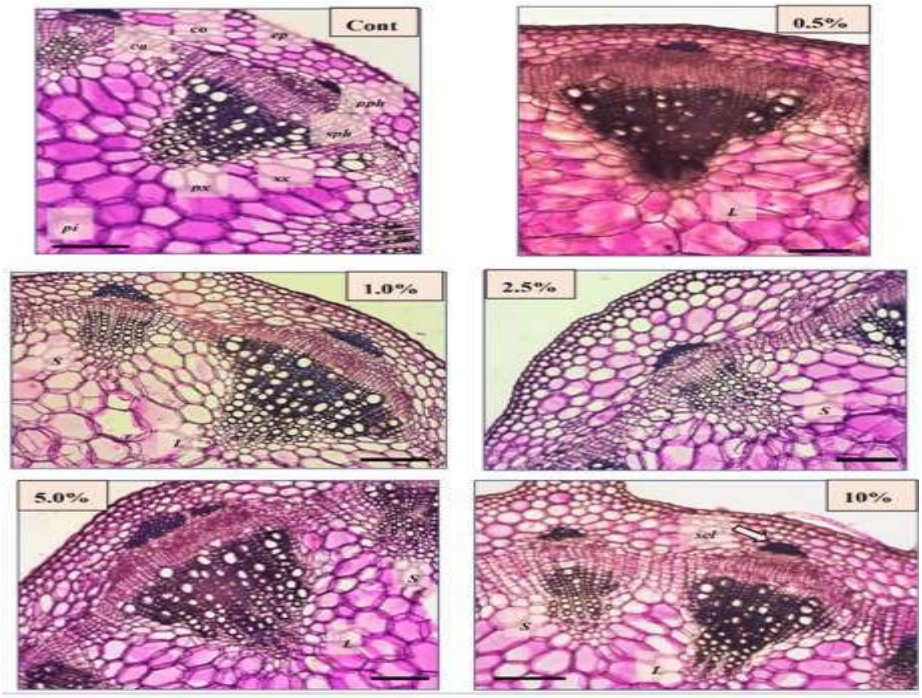
Kingdom : Plantae
Order : Asterales
Family : Asteraceae
Subfamily : Asteroideae
Class : Magnoliopsida
Division : Magnoliophyta
Genus : Tagetes
Species : erecta

Morphological Characters

Marigolds can be either annual or perennial. The marigold stem is upright or branching, and its leaves are dark green and glossy, with opposed or alternating arrangements. [29] The marigold stem is 12 to 30 inches tall. Marigold flowers can be solitary or clustered, and they are bright yellow, orange, or red when simple or pinnately split. [30]

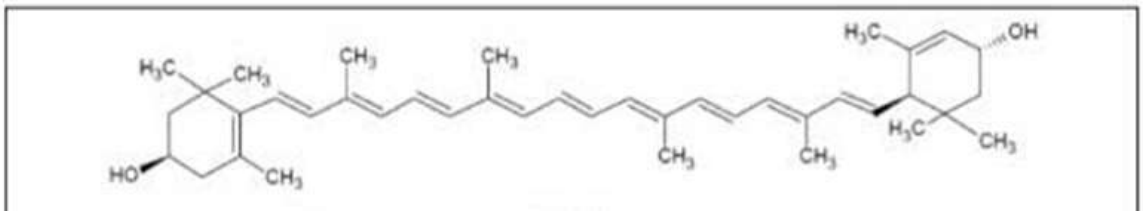
Microscopic Characters

Features of Microscopic Marigold's transverse section demonstrates the structure of leaves In order to prevent water loss, the leaf surface is covered by a single layer of epidermal cells, frequently with a waxy cuticle. Although they are found on both the upper and lower epidermis, stomata are usually more prevalent on the lower side. Spongy mesophyll and palisade make up mesophyll, the internal leaf tissue. [31] Under a microscope, the xylem and phloem tissue found in veins is visible as a vascular bundle. Epidermis: Stem's outermost layer is made up of epidermal cells. Cortex: The parenchyma cells that make up the cortex, which lies beneath the epidermis, may retain starch. Structure of a flower: petals Usually spherical ovules, stamens are specialized cells for producing pigment and may be found in the thickly epidermis petals. Ovules can be seen inside the ovary. Marigold pollen grains are typically spherical, while species-specific variations exist in size and surface roughness. [32]

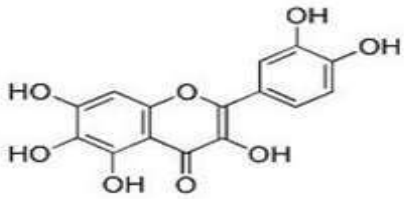


Phytochemical constituents

Phytochemical analyses of its constituent parts have allowed for the isolation of a number of chemical components, including as thiophenes, flavonoids, carotenoids, and triterpenoids. [33] You can find quercetagetin and its glucoside among the recognised residues in T. erecta. It is one of the most important parts of Tagetes erecta and the main pigment, according to Dixit et al. (2013). The flower contains several carotenoids. [34-35]



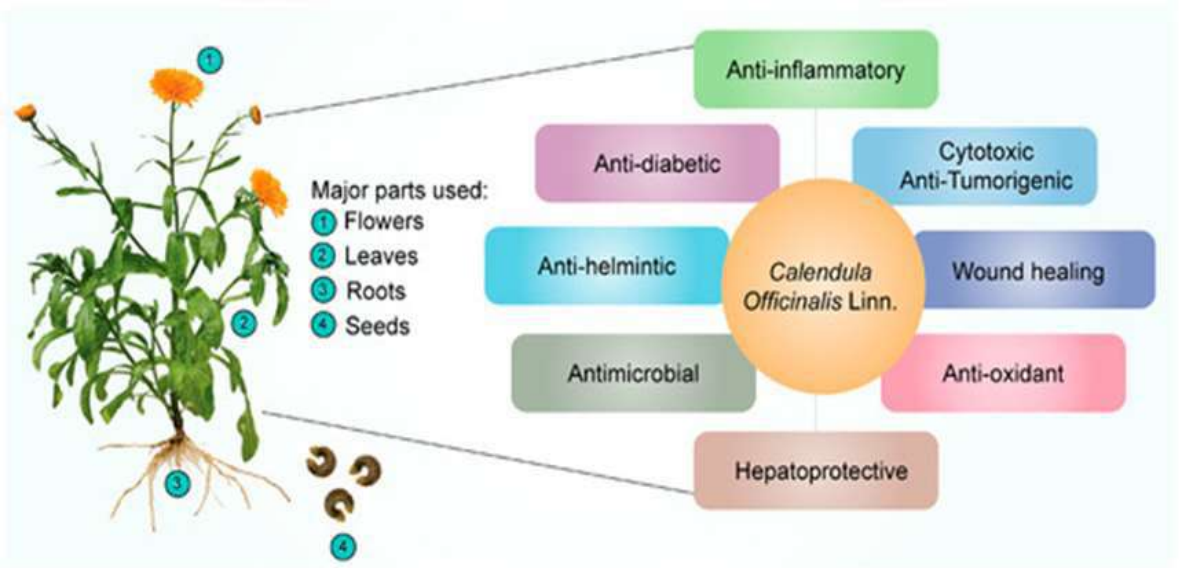
Lutein



Quercetagetin

Medicinal uses

1. Anti-inflammatory reduce inflammation and pain.
2. Antioxidant protect against cell damage.
3. Anticancer inhibit tumor growth and induces apoptosis.
4. Wound healing: topical application for cuts, burns, and ulcers.
5. Digestive issues: relieves constipation, diarrhea and indigestion.
6. Antimicrobial
7. Also used in eye problems respiratory issues, cardiovascular health, menstrual disorder.



MECHANISM

1. One of the many therapeutic uses for the marigold plant is its anti-cancer properties. The anti-cancer and elastase/tyrosinase enzyme inhibitory properties of marigold flower extracts in ethanol and ethyl acetate are well-documented. Cancers of the colon and lung have been found to be resistant to these two extracts. [36]
2. Anti-oxidant activity- Three tests for antioxidant activity were conducted on ethanolic extract of marigold (Tagetes erecta) flowers: reducing power, DPPH & superoxide radical scavenging. Tagetes erecta outperforms conventional ascorbic acid in terms of reducing power, but showing lower than average DPPH antioxidant & superoxide anion scavenging activities. Additionally, Tagetes erecta flower essential oil reveals [37]
3.The antioxidant action of marigold is typically attributed to carotenoids, such as luteins. The healing properties of marigold have made it an ancient medicinal herb. An investigation was conducted into the cytotoxic activity and inhibitory effects of marigold flower extracts in ethanol and ethyl acetate on the elastase and tyrosinase enzymes. Two cancer cell lines: the H460 lung cancer and the $CaCO_2$ colon cancer were used. Compounds known as antioxidants can aid in cellular protection against free radical damage. The extract dramatically increases blood and liver glutathione levels.
4. Induction of Apoptosis: Marigold extracts can promote programmed cell death (apoptosis) in cancer cells. This process may be mediated by the activation of caspases & modulation of apoptotic signaling pathways. [38]
5. Cell Cycle Arrest: Certain compounds in marigolds can interfere with the cell cycle, causing cancer cells to halt their proliferation. For example, they may induce arrest at specific phases of the cell cycle, preventing cancer cells from dividing and growing

In Vivo Studies

The in vivo effects of starting, continuing, and stopping treatments with marigold and basil essential oils on the quantity of EACC (all, dead, and viable), survival of tumor-transplanted female mice, and LDH activity in the tumour cell suspension supernatant. The control group without tumour treatment had an average survival time of 14±0.45 days. The MST of tumor-transplanted female mice was found to be considerably ($p<0.05$) higher after receiving various essential oils of marigold and basil compared to the tumour control group. The current investigation indicated that essential oils of marigold and basil were more effective before treatment began than during or after therapy began. in the text. The marigold and beginning treatments had the longest mean survival times (in days), at 48 and 37.17 days, respectively, while the basil treatments had the shortest at 34 and 30 days, respectively. The MST of tumour transplanted rats showed few impacts from medications administered after the transplant had begun. The group who took marigolds before starting the treatment had the greatest increase in longevity (242.86%).

In vitro Studies

Research conducted using in vitro methods; Assay for cell proliferation and survival: This study employed three distinct cancer cell lines: HL-60 and NB4, which are derived from human promyelocytic leukaemia, and EACC, which are derived from experimental animal's model cancer cells. Cell lines HL-60 and NB4, which were acquired from the American Type Culture Collection (ATCC), were cultured for 24 hours in RPMI 1640 medium that was supplemented with 10% foetal bovine serum (FBS), 2 mmol/L glutamine, penicillin (100 U/ml), and streptomycin (100 µg/ml) in a humidified environment with 5% CO2. We counted the cells. A density of 3×10^3 cells/ml was used for seeding HL-60 and NB4 cells. Following this, the cells were exposed to varying amounts of marigold and basil essential oils to achieve final concentrations of 25, 50, 75, 100, and 200 µg/ml. They were then left to incubate under the identical conditions for an additional day. The amount of fluid containing 1% DMSO was increased until each experiment reached a final volume of 100 µl. The vehicle dimethyl sulfoxide concentration was kept constant for the control cells. The trypan blue assay was used to assess cell viability after this time. In accordance with Bennett et al. (1976), the viability percentages were computed. The capacity of trypan blue dye to provide a blue stain onto the dead cells was crucial to this technique. Then a hemocytometer slide was utilised (under a microscope) for simple counting. Triplicates of each experiment were performed. At the National Cancer Institute (NCI) in

Cairo, Egypt, female Swiss albino mice were used to maintain the Experimental Animal Model Cancer Cell Line (EACC) through weekly intraperitoneal (1p) injection of 2.5 x 106 cells. Our division followed a similar procedure for the identical cells. After 7 days following tumour transplantation, cells were harvested from the animals and counted using the proper microscopy technique to determine the number of cells/ml. This number was then used for both in vivo and in vitro experiments. Before being rinsed with saline, the cells were spun at 1000 rpm for 5 minutes.

Toxicology study

1. Acute Toxicity Research:

- In mice, a 50% mortality rate was observed at an intraperitoneal lethal dose (LD50) ranging from 5 to 7 g/kg, while oral doses between 10 and 13 g/kg caused similar results.
- Oral administration of 5 g/kg in rats resulted in no fatalities.

2. Sub-chronic Toxicity Research:

- During a 90-day oral toxicity study, rats receiving 1000 mg/kg/day exhibited no adverse effects.
- A 28-day dermal toxicity study in rabbits also found no notable irritation or toxicity at a dosage of 1000 mg/kg/day.

3. Chronic Toxicity Research:

- In a six-month oral study, rats administered 500 mg/kg/day showed no signs of cancer development.
- Over a 12-month period, dogs given 200 mg/kg/day orally did not experience any harmful effects.

4. Genotoxicity Research:

- The Ames test yielded negative results, indicating no mutagenic activity.
- The micronucleus test also came back negative, suggesting no chromosomal damage (non-clastogenic).

5. Reproductive Toxicity Studies:

- In a teratogenicity study on rats, daily doses of 1000 mg/kg did not cause fetal abnormalities.
- A separate reproductive toxicity study in rats using 500 mg/kg/day showed no negative impacts on fertility or reproductive function.

6. Hypersensitivity and Allergic Reactions:

- Occasional cases of allergic contact dermatitis have been reported.
- No systemic allergic or hypersensitivity reactions have been documented.

CONCLUSION

The current study underscores the significant anticancer potential of *Tagetes erecta* (marigold), attributed to its rich phytochemical profile, particularly flavonoids and carotenoids such as lutein. Both in vitro and in vivo models show that the plant has substantial cytotoxic, antioxidant, and pro-

apoptotic effects, particularly when taken before the start phase. Furthermore, it has a long history of usage in traditional medicine and has shown to be safe in toxicity trials, lending credence to the idea that it could be a useful anticancer agent. To confirm the therapeutic effectiveness of marigold and make it easier to include it into standard cancer treatment regimens, additional research is needed to isolate specific bioactive components and conduct clinical trials.

REFERENCE

1. Barhoi D, Upadhaya P, Barbhuiya SN, Giri A, Giri S. Aqueous extract of Moringa oleifera exhibit potential anticancer activity and can be used as a possible cancer therapeutic agent: a study involving in vitro and in vivo approach. Journal of the American College of Nutrition. 2021 Jan 2;40(1):70-85.
2. Golias CH, Charalabopoulos A, Charalabopoulos K. Cell proliferation and cell cycle control: a mini review. International journal of clinical practice. 2004 Dec;58(12):1134-41.
3. Torre LA, Siegel RL, Ward EM, Jemal A. Global cancer incidence and mortality rates and trends—an update. Cancer epidemiology, biomarkers & prevention. 2016 Jan 1;25(1):16-27.
4. Cao W, Chen HD, Yu YW, Li N, Chen WQ. Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020. Chinese medical journal. 2021 Apr 5;134(7):783-91.
5. Fitzgerald RC, Antoniou AC, Fruk L, Rosenfeld N. The future of early cancer detection. Nature medicine. 2022 Apr;28(4):666-77.
6. Malabadi RB, Sadiya M, Kolkar KP, Mammadova SS, Chalannavar RK, Baijnath H. Role of Plant derived-medicine for controlling cancer. Int. J. Sci. Res. Arch. 2024;11(1):2502-39.
7. Garcia-Oliveira P, Otero P, Pereira AG, Chamorro F, Carpena M, Echave J, Fraga-Corral M, Simal-Gandara J, Prieto MA. Status and challenges of plant-anticancer compounds in cancer treatment. Pharmaceuticals. 2021 Feb 14;14(2):157.
8. Brown JM, Wouters BG. Apoptosis, p53, and tumor cell sensitivity to anticancer agents. Cancer research. 1999 Apr 1;59(7):1391-9.
9. Newman DJ, Cragg GM, Snader KM. The influence of natural products upon drug discovery. Natural product reports. 2000;17(3):215-34.
10. Kalemba DA, Kunicka A. Antibacterial and antifungal properties of essential oils. Current medicinal chemistry. 2003 May 1;10(10):813-29.
11. Salehi B, Valussi M, Morais-Braga MF, Carneiro JN, Leal AL, Coutinho HD, Vitalini S, Kręgiel D, Antolak H, Sharifi-Rad M, Silva NC. Tagetes spp. essential oils and other extracts: Chemical characterization and biological activity. Molecules. 2018 Nov 1;23(11):2847.
12. Shikha D, Kashyap P. Ocimum species. Harvesting food from weeds. 2023 Jul 21:183-215.
13. Rawla P, Sunkara T, Gaduputi V. Epidemiology of pancreatic cancer: global trends, etiology and risk factors. World journal of oncology. 2019 Feb 26;10(1):10.
14. Gómez de Cedrón M, Mouhid L, García-Carrascosa E, Fornari T, Reglero G, Ramírez de Molina A. Marigold supercritical extract as potential co-adjuvant in pancreatic cancer: the energetic catastrophe induced via BMP8B ends up with autophagy-induced cell death. Frontiers in Bioengineering and Biotechnology. 2020 Jan 24; 7:455.
15. Kleeff J, Korc M, Apte M, La Vecchia C, Johnson CD, Biankin AV, Neale RE, Tempero M, Tuveson DA, Hruban RH, Neoptolemos JP. Pancreatic cancer. Nature reviews Disease primers. 2016 Apr 21;2(1):1-22.
16. Smeenk HG, Tran TC, Erdmann J, Van Eijck CH, Jeekel J. Survival after surgical management of pancreatic adenocarcinoma: does curative and radical surgery truly exist? Langenbeck's archives of surgery. 2005 Apr; 390:94-103.
17. Kalofonos HP, Aravantinos G, Kosmidis P, Papakostas P, Economopoulos T, Dimopoulos M, Skarlos D, Bamias A, Pectasides D, Chalkidou S, Karina M. Irinotecan or oxaliplatin combined with leucovorin and 5-fluorouracil as first-line treatment in advanced colorectal cancer: a multicenter, randomized, phase II study. Annals of oncology. 2005 Jun 1;16(6):869-77.
18. Sultana S, Khan A, Safhi MM, Alhazmi HA. Cough suppressant herbal drugs: A review. Int. J. Pharm. Sci. Invent. 2016 Aug;5(5):15-28.

19. Kar S, Patra S. A Review on Marigold (Tagetes erecta Linn): the Phytochemicals Present and its Biological activities. Pray Rasayan. 2022;6(4):50-8.
20. Wanzala W, Wagacha JM, Dossaji SF, Gakuubi MM. Bioactive properties of Tagetes minuta L. (Asteraceae) essential oils: A review.
21. Neher RT. The ethnobotany of Tagetes. Economic Botany. 1968 Oct 1:317-25.
22. Salehi B, Valussi M, Morais-Braga MF, Carneiro JN, Leal AL, Coutinho HD, Vitalini S, Kręgiel D, Antolak H, Sharifi-Rad M, Silva NC. Tagetes spp. essential oils and other extracts: Chemical characterization and biological activity. Molecules. 2018 Nov 1;23(11):2847.
23. Gupta YC, Panwar S, Banyal N, Thakur N, Dhiman MR. Marigold. InFloriculture and Ornamental Plants 2022 Jul 6 (pp. 1-23). Singapore: Springer Nature Singapore.
24. Gupta YC, Panwar S, Banyal N, Thakur N, Dhiman MR. Marigold. InFloriculture and Ornamental Plants 2022 Jul 6 (pp. 1-23). Singapore: Springer Nature Singapore.
25. Sievers AF, Higbee EC. Medicinal plants of tropical and subtropical regions. US Department of Agriculture; 1942.
26. 09Barhoi D, Upadhaya P, Barbhuiya SN, Giri A, Giri S. Extracts of Tagetes erecta exhibit potential cytotoxic and antitumor activity that could be employed as a promising therapeutic agent against cancer: A study involving in vitro and in vivo approach. Phytomedicine Plus. 2022 Feb 1;2(1):100187.
27. Marino P. Isolation, characterization and biological evaluation of onconutraceuticals compounds in the Mediterranean area: new tools for the treatment of oncological diseases.
28. Saini I, Chauhan J, Kaushik P. Medicinal value of domiciliary ornamental plants of the Asteraceae family. Journal of young pharmacists. 2020;12(1):3.
29. Brickell C. RHS encyclopedia of plants and flowers. Dorling Kindersley Ltd; 2019 Oct 3.
30. Gupta YC, Panwar S, Banyal N, Thakur N, Dhiman MR. Marigold. InFloriculture and Ornamental Plants 2022 Jul 6 (pp. 1-23). Singapore: Springer Nature Singapore.
31. Naidoo Y, Rikisahedew JJ, Dewir YH, Ali AA, Rihan HZ. Foliar micromorphology, ultrastructure and histochemical analyses of Tagetes minuta L. leaves. Micron. 2021 Nov 1; 150:103125.
32. Crang R, Lyons-Sobaski S, Wise R, Crang R, Lyons-Sobaski S, Wise R. Parenchyma, collenchyma, and sclerenchyma. Plant Anatomy: A Concept-Based Approach to the Structure of Seed Plants. 2018:181-213.
33. Ibrahim SR, Abdallah HM, El-Halawany AM, Mohamed GA. Naturally occurring thiophenes: isolation, purification, structural elucidation, and evaluation of bioactivities. Phytochemistry reviews. 2016 Apr; 15:197-220.
34. Khulbe A. A review on Tagetes Erecta. World Journal of Pharmaceutical Sciences. 2015 Mar 5:645-9.
35. Olennikov DN, Kashchenko NI. Marigold metabolites: Diversity and separation methods of Calendula genus phytochemicals from 1891 to 2022. Molecules. 2022 Dec 6;27(23):8626.
36. John JN, Mascarenhas RA, Gangadhara V, Abraham A. Floral pigments and its cytotoxic activity: An update. Indian Journal of Natural Products and Resources (IJNPR)[Formerly Natural Product Radiance (NPR)]. 2024 Apr 26;15(1):43-53.
37. Umar S, Sharma MP, Khan W, Ahmad S. Variation in ornamental traits, physiological responses of Tagetes erecta L. and T. patula L. in relation to antioxidant and metabolic profile under deficit irrigation strategies. Scientia Horticulturae. 2017 Jan 5; 214:200-8.
38. Creagh EM, Conroy H, Martin SJ. Caspase-activation pathways in apoptosis and immunity. Immunological reviews. 2003 Jun;193(1):10-21.
39. Mahmoud GI. Biological effects, antioxidant and anticancer activities of marigold and basil essential oils. J. Med. Plants Res. 2013 Mar 10;7(10):561-72.
40. Li Y, Li L. Contact dermatitis: classifications and management. Clinical reviews in allergy & immunology. 2021 Dec;61(3):245-81.

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