

An evidence-based update on the pharmacological activities of *Tagetes patula*

Parth Rastogi¹ and Parmesh Kumar Dwivedi^{1*}

¹Amity Institute of Pharmacy, Lucknow, Amity University Uttar Pradesh, Sector 125, Noida-201313, India

*Corresponding author: E-mail: parmeshdwivedi@gmail.com, pkdwivedi@lko.amity.edu

Corresponding author

Dr. Parmesh Kumar Dwivedi
Associate Professor
Amity Institute of Pharmacy, Lucknow,
Amity University Uttar Pradesh,
Sector 125, Noida-201313, Uttar Pradesh (India)
parmeshdwivedi@gmail.com

Abstract

The present review has focused the traditional uses of Tagetes patula across the globe. The pharmacological potential of T. patula was explored. It has been found to be effective in fever, ear aches, ophthalmia and muscular pain. In the recent years several biological potentials of Tagetes patula plant have been investigated which includes anti-microbial, anti-oxidant, anti-inflammatory, anti-arthritis, anti-diabetic and anti-thrombotic. The wide spectrum of therapeutic activities also includes hepatoprotective, neuroprotective, analgesic and cardio protective activities. This species of marigold is also used as crop protectant and have larvicidal and nematicidal potential hence can be uses as fertilizer in crops. Researches are still in progress to enhance the pharmacology of the plant. In the present review an attempt has been made to compile and update the medicinal importance of this plant. The antibacterial, antifungal, antiviral and anti-oxidant potential of this plant has already been reviewed in our previous work. The present review has been made to explore other pharmacological activities to help the researchers to find new insights for further investigation on this plant.

Keywords: *Tagetes patula, anti-inflammatory, anti-diabetic, Immunomodulatory, cytotoxic*

Introduction

Tagetes plant with more than 55 species have different chemical and medicinal properties, and can generate the compounds with great pharmaceutical and nutritional importance. *Tagetes patula* L. plant has been very common ornamental plant but it also has a wide range of pharmacological properties. This France marigold, is a single-year plant which synthesizes similar ingredients like *T. minuta* but also has patuletin and patulitrin, rare antimicrobial and anti-inflammatory chemicals. It is widely distributed across the world and is used for various different purposes as traditionally as well as medicinally active plant. Nowadays, researchers are more interested in finding pharmaceutical equivalents of traditional uses of medicinal plants, as well as the semisynthetic derivatives of their potential chemical constituents. (Chaturvedi et al., 2015).

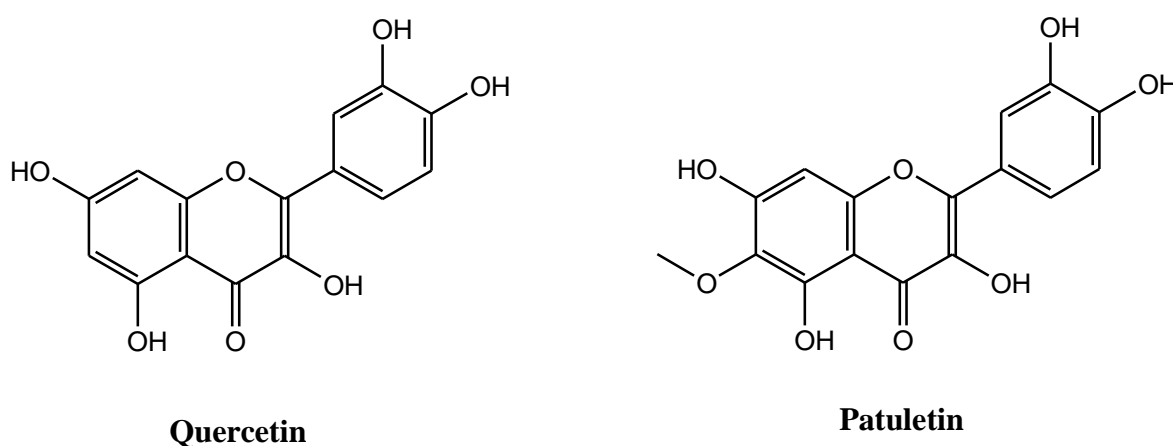


Figure 1: Quercetin and Patuletin (The constituents of *Tagetes patula*)

African or American Marigolds (*Tagetes erecta*), French Marigolds (*Tagetes patula*), Signet Marigolds (*T. signata* 'pumila') and Mule Marigolds are some of the important *Tagetes* varieties. The present review is highlighted on various pharmacological activities of *Tagetes patula*. Various pharmacological activities have been reported, the details of which are presented below:

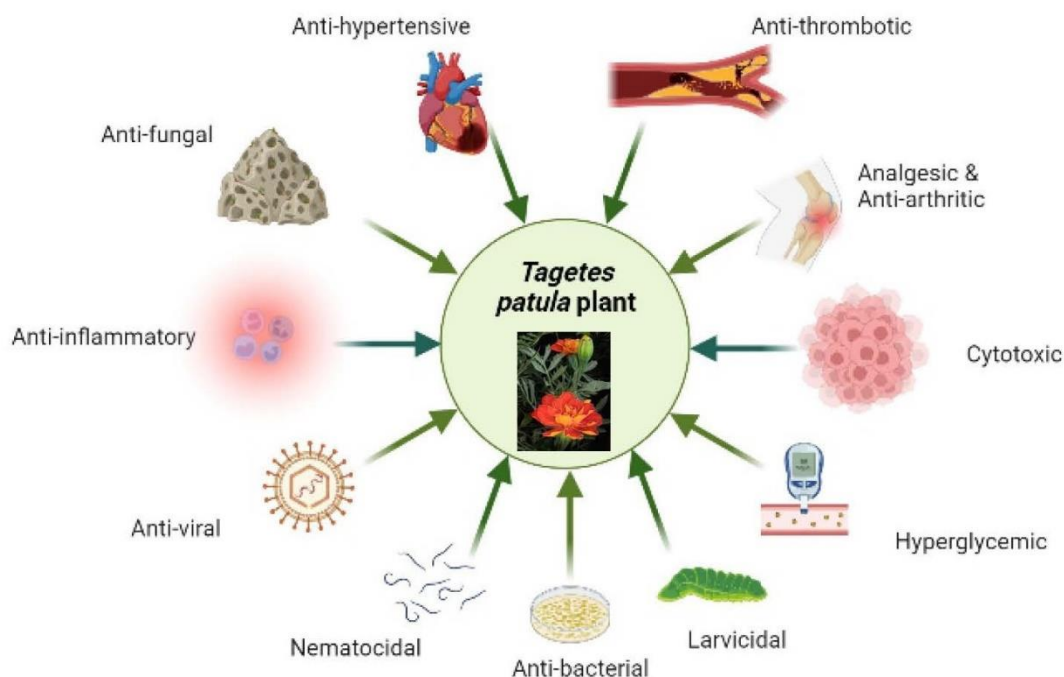


Figure 2: Pharmacological activities of *Tagetes Patula*

1. Anti-inflammatory potential

The extract of *Tagetes patula* prepared with water was reported to be effective in the treatment of prostatitis in rats. The decoction of water was prepared with the plant and was evaluated against nonbacterial prostatitis via model of estradiol induced subcutaneously in castrated male rats. Results depicted decrease in the level of IL-1 β , TNF- α , and EGF and enhanced levels of testosterone and dihydrotestosterone which down-regulates the symptoms of prostatitis (Liu et al., 2017).

2. Cytotoxic potential

Tagetes patula flowers have been evaluated for the treatment of cancer cells. The methanolic extract and ethyl acetate extract were evaluated for cytotoxic actions via the root length inhibition and mitotic index with the help of *Allium* test. Hence it has been proved to have a cytotoxic action but clinical studies are required for the treatment against the human cancer cell lines (Azhar et al., 2019). The methanolic extract of *Tagetes patula* flower was observed to contain some phenolic compounds and was evaluated on HeLa, MCF-7, PC-3 and SF-268 human cancer cell lines via sulforhodamine-B assay for cytotoxic activity. The methanolic extract was earlier observed for anti-oxidant activity. It was observed that it contains some phenolic compounds such as methyl prorocatechuate, patuletin, and patulitrin which were tested for cytotoxic activity on different human cancer cell lines. Cancer cell lines used were large carcinoma lung cells (NCI-H460), prostate cancer cells (PC-3), uterine cervix cancer cells (HeLa), anaplastic astrocytoma CNS (SF-268), and breast cancer cells

(MCF-7). Results obtained showed cytotoxic activity in the human cancer cell lines because of the presence of phenolic compounds (Kashif et al., 2015).

3. Analgesic potential

Patuletin and patulitrin were found to be the major compounds isolated from the petals or florets of *Tagetes patula*. According to a research oral administration of methanol extracts of *Tagetes patula* containing patuletin and patulitrin show inhibitory activity in acute inflammation cases. This was investigated by various animal models such as γ -carrageenin induced hind paw oedema, histamine induced hind paw oedema, and arachidonic acid induced ear oedema. Hence, the flavonoids patuletin and patulitrin present in French marigold shows inhibitory activity against acute inflammation and a potent analgesic activity (Yasukawa et al., 2013). The research performed by Faizi *et al.* demonstrated the antioxidant and analgesic activity of *Tagetes patula* flower methanolic extract. The compounds responsible for antioxidant activity were methyl protococatechuate, patuletin, and patulitrin. Among these compounds patuletin depicts analgesic activity. The flavonoids patuletin and patulitrin were isolated by solvent- solvent extraction method and pure form of patuletin was tested for analgesic activity. Acetic acid induced writhing test and hot plate test in mice were used to evaluate the analgesic activity which proved to be successful (Faizi et al., 2011). The florets of *Tagetes patula* were investigated for chronic inflammation activity via carrageenin induced paw oedema in rats and mice. The methanolic extract in the form of oral dose was administered to rats and mice. Thereafter, it was observed that the methanolic extract of florets of *Tagetes patula* at the dose of 400mg/kg was effective against oedema in the hind paw. This was because of enhanced vascular permeability because of a flavonoid patuletin. Hence, it was effective in acute inflammation and slightly potent against chronic inflammation (Kasahara et al., 2002).

4. Immunomodulatory potential

The flowers of *Tagetes patula* were evaluated for the treatment of inflammation related disorders by the protection of Jurkat T-cells from oxidative stress. It was observed that the flavonoids present in the plant such as patuletin, quercetagenin, and quercetin play a vital role in the production of inflammatory mediators and antioxidant interleukins-10 which prevents oxidative stress in the Jurkat T-cells (Chkhikvishvili et al., 2016).

5. Hyperglycemic potential

The leaves of *Tagetes patula* methanolic extract has been proven to decrease the trehalose level in the body of *Dorsophila*. Due to the dip in the trehalose level, it may be proven to have a potential anti-diabetic effect (Elbrense et al., 2021). According to the research by Sathi *et al.* the stems of *Tagetes patula* were evaluated for the diabetic potential and anti-nociceptive potential. The different doses of the methanolic extract of the stem of *Tagetes patula* i.e. 50, 100, 200, and 400 mg/kg doses were compared with 10mg glibenclamide and the highest dose was favourable with their respective standard drug. The mechanisms were not elaborated but as expected that for anti-hyperglycaemic activity it may be due to

inhibition of glucose absorption in gut, increased pancreatic secretion or increased glucose uptake, and may be due to peripheral glucose consumption is enhanced. Anti-nociceptive action may be due to inhibition of cyclo-oxygenase (COX) and lipo-oxygenase (LOX) enzyme that may lead to decreased prostaglandin secretion and this was compared with aspirin. Hence anti-diabetic and anti-nociceptive activities were evaluated (Sathi et al., 2012).

6. Anti-hyperlipidaemic potential

According to Nawale *et al.* (2018) the methanolic extract of *Tagetes patula* was evaluated against hyperlipidaemia induced via propylthiouracil and triton-X100. It was observed that under the influence of piperine the methanolic extract of *Tagetes patula* show changes in the lipid profile and according to the histopathological changes it depicts anti-hyperlipidemic activity (Nawale et al., 2018).

7. Anti-hypertensive potential

Tagetes patula a very common ornamental plant was evaluated for the anti-hypertensive activity with the methanolic extract of its roots. Sprague-Dawley rats were taken and their arterial blood pressure was measured from the carotid artery. The methanolic extract of *Tagetes patula* roots when administered, recorded a fall in mean arterial blood pressure at doses of 3mg/kg and 30mg/kg. The chemical compounds which were found to be responsible for hypotensive action were citric acid and malic acid with 71% and 43% fall in blood pressure respectively (Saleem et al., 2004).

8. Anti-arthritic potential

According to Jabeen *et al.* (2016), *Tagetes patula* was evaluated for the anti-arthritic potential. It was observed that it contains a chemical compound patuletin which showed the inhibition of TNF- α and IL-1 β due to which inflammation in the knees was inhibited. Fresh *Tagetes patula* flowers were collected and a flavonoidal compound named patuletin was isolated and it was tested by the method of induction of adjuvant induced arthritis. It was observed that it inhibited the production of pro inflammatory cytokines TNF- α and IL-1 β . According to the histopathology of knee joints in rats it was observed that animal receiving patuletin as a treatment regime showed anti-arthritic potential (Jabeen et al., 2016). According to MT Khan (1996) in the research article the tincture of *Tagetes patula* was used and applied on the bunion joint and observed for the treatment of hallux abducto valgus and its associated conditions such as arthritis and inflammation. This study was conducted as double-blind placebo controlled trial for the duration of eight weeks. The number of patients used in this trial was sixty out of which 20 patients suffered from bilateral hallux abducto valgus and 40 patients selected were having unilateral hallux abducto valgus. Results were obtained and evaluated by photographs and radiographs. Results show relief in pain and reduction of soft tissue in all subjects and partial correction of angle and reduction in swelling of joint. This depicts a protective effect of French marigold in podiatric treatment of hallux abducto valgus (Khan, 1996).

9. Diuretic potential

According to Lui *et al.* (2019) *Tagetes patula* was investigated against chronic non-bacterial prostatitis mechanism. It was observed that the polysaccharides and flavonoids present in *Tagetes patula* enhance the level of DHT and depreciate the level of PSA and TNF- α . It also initiates the Na⁺/K⁺-ATPase activity which regulates the energy metabolism in liver and prostate and energy production and respiratory exchange was also promoted. Hence, by reduction of inflammation factors and regulation of metabolism of amino acids, energy, glucose and lipid it depicts anti-chronic non-bacterial prostatitis activity (Lui *et al.*, 2019).

10. Neuroprotective potential

In a recent research article the flower and whole plant of *Tagetes patula* was taken and different chemical compounds were isolated and were evaluated for the neuroprotective action on the injury of human neuroblastoma SH-SY5Y cells. The compounds isolated from marigold with respect to capacity of neuroprotective action were biflavone with highest activity, patuletin, quercetin, kaempferol-3-O- β -D- glucoside, and patuletin-3-O- α -L-arabinopyranoside with lowest activity. Hence, conclusion obtained from this research was flavonoids present in *Tagetes patula* show neuro-protecting activity against SH-SY5Y cells which are induced by glutamate (Lui *et al.*, 2020). Alzhemiers disease treatment is still done with the help of acetylcholine esterase inhibitors. Hence, it was reported that ethanolic extract of *Tagetes patula* was effective against the cognitive impairment by scopolamine induced amnesia in mice model. Behavioural changes were assessed through the passive avoidance apparatus and the water maze apparatus. Results obtained show decreased escape latency in water maze test and increased latency time. Treated mice show increased level of superdioxide dismutase, dopamine, glutathione reductase, and serotonin and decreased level of lipid peroxidation which depicts the anti-amnesic effect (Ramakrishnan *et al.*, 2015).

11. Antithrombotic potential

The leaf of *Tagetes patula* with different extracts of methanol, n-hexane, chloroform and carbon tetrachloride were evaluated for thrombolytic and anti-bacterial activity. It was observed that the n-hexane extract of leaf was most effective for thrombolytic activity as it prevent the formation of blood clot and also leads to the lysis of the clot formed in the blood. This activity was done with standards as streptokinase and water as positive and negative control respectively (Kuddus *et al.*, 2012).

12. Hepatoprotective potential

The flavonoids extracted form the seeds of *Tagetes patula* have been identified to be used as a traditional medicine for the protection of liver and hence can be used as hepatoprotective agent (Kshirsagar *et al.*, 2011).

13. Larvicidal potential

Larvicidal activity in a plant may be helpful to eliminate dengue fever as there is no such specific medication for dengue hence to fight against dengue it is better to eliminate the principle vector *Aedes aegypti*. According to a research article crude acetone extract of inflorescences of *Tagetes patula* was found to be active against the *Aedes aegypti* vector. Crude acetone extract was divided into five different extracts of hexane, dichloromethane, aqueous, ethyl acetate and n-butanol amongst which ethyl acetate extract have highest larvicidal activity because of high concentration of patuletin (Krzyzaniak et al., 2017). According to Munhoz *et al.* (2014) different extracts of flowers of *Tagetes patula* were evaluated for larvicidal activity. Due to the presence of flavonoids, the acetone extracts depicted highest activity at 1ppm concentration against *Aedes aegypti* to show larvicidal activity (Munhoz et al., 2014). Dharmagadda *et al.* (2005) reported the larvicidal activity of essential oils of *Tagetes patula* against different larvae. The average yield of essential oils was found to be 1.5% containing certain compounds such as terpinolene, dihydrotageton, limonene, piperitone, caravone, β -ocimene, and α -pipene. These compounds have been found to cause mortality of the larvae of *Aedes aegypti*, *Anopheles stephensi*, and *Culex quinquefasciatus* (Dharmagadda et al., 2004). The reported evidence depicted the larvicidal activity against certain larvae by the leaf tissue of *Tagetes patula*. The leaves of *Tagetes patula* are rich in thiophenes and its callus culture has been reported to show larvicidal activity against *Aedes aegypti*, *Anopheles stephensi*, and *Culex quinquefasciatus* larvae (Rajasekaran et al., 2004).

14. Nematicidal potential

According to a recent study it has been suggested that *Tagetes patula* can be used as a cover crop in nematode management. It has been an effective plant in suppressing the root-knot nematode. It suppresses *Pratylenchus penetrans* and *Pratylenchus pratensis* nematode and also enhances the yield of *Colocastia esculenta* crop (Karkas and Bolukbasi, 2019). According to a research it was reported that by inducing hairy roots in *Tagetes patula* with the help of *Agrobacterium rhizogenes* produces some compounds which are responsible for the nematicidal activity. HPLC technique analysis report suggested that α -terthienyl was produced by the hairy roots which is effective in nematicidal activity (Kyo et al., 1990).

Conclusion

French marigold (*Tagetes patula*, Family: Asteraceae) has a wide range of pharmacological activities and has been established to be an effective source against various ailments. According to earlier researches it was established that marigold has been used as an ornamental garland plant but over years it has been used as anti-bacterial, anti-fungal, anti-oxidant, anti-hypertensive, anti-diabetic, anti-hyperlipidemic, and as hepatoprotective and neuroprotective agent. It has been researched that it has a cytotoxic activity and can be used against different types of cancer cells such as lung cancer cells, breast cancer cells, liver cancer cells, uterine cancer cells, and prostate cancer cells. It also possesses some immunomodulatory activity.

Conflict of Interest

All authors declare no conflict of interest.

References

1. Chaturvedi D, Dwivedi PK, Chaturvedi AK, Mishra, N, Siddiqui HH, Mishra V, Semisynthetic hybrids of boswellic acids: a novel class of potential anti- inflammatory and anti-arthritic agents. *Med Chem Res.* 2015, 24, 2799-2812.
2. Liu X, Ran X, Dou D, Cai D. Effectiveness of *Tagetes patula* against chronic nonbacterial prostatitis in rat model. *Bangladesh Journal of Pharmacology.* 2017 Oct; 12(4): doi: 376-383. 10.3329/bjp.v12i4.33240
3. Azhar M, Farooq AD, Haque S, Bano S, Zaheer L, Faizi S. Cytotoxic and genotoxic action of *Tagetes patula* flower methanol extract and patuletin using allium test. *Turkish Journal of Biology.* 2019 Oct; 43(5): doi: 326-339. 10.3906/biy-1906-7
4. Kashif M, Bano S, Naqvi S, Faizi S, Lubna, Mesaik MA, Azeemi KS, Farooq AD. Cytotoxic and antioxidant properties of phenolic compounds from *Tagetes patula* flower. *Pharmaceutical Biology.* 2015 May; 53(5): 672-681. doi: 10.3019/13880209.2014.936471
5. Yasukawa K, Kasahara Y, Effect of flavonoid from French marigold (Florets of *Tagetes patula* L.) on acute inflammation. *International Journal of Inflammation.* 2013 Sep; 1-5. doi: 10.1155/2013/309493
6. Faizi S, Dar A, Siddiqi H, Naqvi S, Naz A, Bano S, Lubna. Bioassay- guided isolation of antioxidant agents with analgesic properties from flowers of *Tagetes patula*. *Pharmaceutical Biology.* 2011 May; 49(5): 516-525. doi: 10.3109/13880209.2010.532006
7. Kasahara Y, Yasukawa K, Kitanaka S, Khan MT, Evans FJ. Effect of methanol extract form flower petals of *Tagetes patula* L. an acute and chronic inflammation model. *Phytotherapy Research.* 2002 May; 16(3): 217-222. doi: 10.1002/ptr.1099
8. Chkhikvishvili I, Sanikidze T, Gogia N, Enukidze M, Machavariani M, Kipiani N, Vinokur Y, Rodov V. Constituents of French marigold(*Tagetes patula* L.) flowers protect Jurkat T-cells against oxidative stress. *Oxidative Medicine and Cellular Longevity.* 2016 Jun; 2016(): 4216285. doi: 10.1155/2016/4216285
9. Elbrense H, Montaser O, El-Aasr M, Meshrif WS. Potential anti-diabetic effect of certain plant extracts from the Egyptian flora on type II diabetes using *Drosophila melanogaster* as an animal model. *International Journal of Cancer and Biomedical Research.* 2021 Oct; 5(4): 121-133. doi: 10.21608/jcbr.2021.90207.1225
10. Sathi SI, Rahman S, Shoyeb MA, Debnath K, Haque MA, Khatun Z, Hossain MS, Shelley MMR, Rahmatullah M. A preliminary study of the anti-hyperglycaemic and anti-nociceptive potential of *Tagetes patula* I. (Asteraceae) stems. *Advances in Natural and Applied Sciences.* 2012 Jan; 6(8): 1515-1520. ISSN: 1995-0772
11. Nawale S, Padma KP, Pranusha P, Ganga MR. Data of anti-hyperlipidaemic activity for methanolic extract of *Tagetes patula* Linn. Flower head along with piperine, as bioavailability enhancer. *Data in Brief.* 2018 Oct; 21(2018): 587-597. doi: 10.1016/j.dib.2018.10.022

12. Saleem R, Ahmad M, Naz A, Siddiqui H, Ahmad SI, Faizi S. Hypotensive and toxicological study of citric acid and other constituents form *Tagetes patula* roots. Archives of Pharmacal Research. 2004 Oct; 27(10): 1037-1042. doi: 10.1007/bf02975428
13. Jabeen A, Mesaik MA, Simjee SU, Lubna, Bano S, Faizi S. Anti-TNF- α and anti-arthritis effect of patuletin: A rare flavonoid form *Tagetes patula*. International Immunopharmacology. 2016 Jul; 36(30): 232-240. doi: 10.1016/j.intimp.2016.04.034
14. Khan MT. The podiatric treatment of hallux abducto valgus and its associated conditions, bunion, with *Tagetes patula*. Journal of Pharmacy and Pharmacology. 1996 Jul; 48(7): 768-770. doi: 10.1111/j.2042-7158.1996.tb03968.x.
15. Lui X, Ran X, Riaz M, Kuang H, Dou D, Cai D. Mechanism investigation of *Tagetes patula* L. against chronic nonbacterial prostatitis by metabolomics and network pharmacology. Molecules. 2019 Jun; 24(12): 2266. doi: 10.3390/molecules24122266
16. Lui L, Luo S, Yu M, Metwaly AM, Ran X, Ma C, Dou D, Cai D. Chemical constituents of *Tagetes patula* and their neuro-protecting action. Natural Products Communication. 2020 Oct; 15(11): 1-8. doi: 10.1177/1934578X20974507
17. Ramakrishnan P, Chandrasekhar T, Muralidharan P. Cognitive enhancing, anti-acetylcholinesterase, and antioxidant properties of *Tagetes patula* on scopolamine-induced amnesia in mice. International Journal of Green Pharmacy. 2015 Jul; 9(3): 167-174. doi: 10.4103/0973-8258.161234
18. Kuddus MR, Alam MS, Chowdhury SR, Rumi F, Sikder MA, Rashid MA. Evaluation of membrane stabilizing activity, total phenolic content, brine shrimp lethality bioassay, thrombolytic and antimicrobial activities of *Tagetes patula* L. Journal of Pharmacognosy and Phytochemistry. 2012 Nov; 1(4): 57-63.
19. Kshirsagar AD, Mohite R, Aggrawal AS, Suralkar UR. Hepatoprotective medicinal plants of ayurveda— A review. Asian Journal of Pharmaceutical and Clinical Research. 2011 July; 4(3): 1-8. doi: 0974-2441.
20. Krzyzaniak LM, Antonelli-Ushirobira TM, Panizzon G, Sereia AL, Pinto de souza JR, Zequi JAC, Novello CR, Lopes GC, Medeiros DC, Silva DB, Leite-Mello EVS, Mello JCP. Larvicidal activity against *Aedes aegypti* and chemical characterization of the inflorescences of *Tagetes patula*. Evidence-Based Complementary and Alternative Medicine. 2017 Oct; 2017(5): 1-8. doi: 10.1016/j.fitote.2005.06.013
21. Munhoz VM, Longhini R, Souza JRP, Zequi JAC, Mello EVSL, Lopes GC, Mello JCP. Extraction of flavonoid from *Tagetes patula*: Process, optimization and screening for biological activity. Brazilian Journal of Pharmacognosy. 2014 Oct; 24(5): 576-583. doi: 10.1016/j.bjp.2014.10.001
22. Dharmagadda VSS, Naik SN, Mittal PK, Vasudevan P. Larvicidal activity of *Tagetes patula* against three mosquito species. Bioresource Technology. 2005 Dec; 96(11): 1235-1240. doi: 10.1016/j.biortech.2004.10.020
23. Rajasekaran T, Ravishankar GA, Reddy BO. Production of thiophene from *Tagetes patula* L. and mosquito larvicidal activity. Indian Journal of Experimental Biology. 2004 Apr; 3(1): 92-96. doi: 10.5897/AJB2015.14483
24. Karakas M, Bolukbasi E. A review: Using marigold (*Tagetes spp.*) as an alternative to chemical nematicide for nematode management. International Journal of Advanced

- Engineering, Management and Sciences. 2019 Sep; 5(9): 556-560. doi: 10.22161/ijaems.59.3
25. Kyo M, Miyauchi Y, Fujimoto T, Mayama S. Production of nematocidal compounds by hairy root cultures of *Tagetes patula* L. Plant Cell Reports. 1990 Nov; 9(7): 393–397. doi: 10.1007/BF00232407