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A Brief Review On Calendula Officinalis In Herbal Medicine

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ABSTRACT
Calendula officinalis, commonly known as marigold, has a rich history in herbal medicine, recognized for its diverse pharmacological activities. The plant, native to Europe and widely cultivated, is utilized in various preparations for its anti-inflammatory, antimicrobial, antioxidant, and wound-healing properties. Its flowers and leaves contain a range of bioactive compounds, including flavonoids, saponins, and terpenoids, which contribute to its therapeutic effects. Traditional uses encompass treatment for skin ailments, infections, and digestive disorders, while modern studies validate its efficacy in managing conditions like diabetes and cardiovascular diseases. The extraction methods and safety profiles of Calendula extracts have shown minimal toxicity, making them viable for herbal formulations. Future research is encouraged to explore the full potential of this versatile herb, including its lesser-studied parts and advanced extraction techniques, to enhance its therapeutic applications in herbal medicine.

Keywords: Mari gold, Calendula Extract, Pharmacological Activity, Phytoconstituent.

INTRODUCTION

Calendula
"Calendula" derives from the Latin "calends," marking the flower's blooming on the first day of each month. It's also called the "herb of the sun" due to its flowers opening in the morning and closing at night [1]. The term "Marigold" in English combines "Mary" and "gold," underscoring the flower's golden colour and its association with St. Mary [2]. Consists of about 25 herbaceous species. Some of the most common species are Calendula officinalis, Calendula arvensis, Calendula suffruticosa, Calendula stellata, Calendula alata, and Calendula tripterocarpa[3]. The World Health Organization (WHO, 2003) reports that around 80% of the global population uses herbal remedies for symptom relief, with at least 30% of these remedies showing medical value [4]. Various Calendula preparations can be used in topical formulations aimed at promoting wound healing and soothing irritated or damaged skin. These include extracts, tinctures, and oils [5]. The yellow or orange flowers are utilized in cosmetics for their nutritional value, colouring properties, flavour, and are also used in taste , lotions, and moisturizers [6]. Marigold plants are easy to cultivate because they can adapt to a variety of soil types and climatic conditions. They are used in modern medicine, and also in the production of nylons and dyes, both in their raw and processed forms [7]. Calendula officinalis is recognized for its medicinal properties in both Ayurvedic and Unani medicine systems[8]. Calendula officinalis was utilized for its anti-inflammatory, diaphoretic, analgesic, and antiseptic properties, as well as for treating jaundice [9]. Calendula ointments are skin care products designed to address minor cuts, burns, and skin irritations [10]. This herb is well-regarded in ancient medicine and is used in traditional and homeopathic treatments [11].

Biological Source
It is obtained from Calendula officinalis flowers by steam distillation [12].

Organoleptic properties
Odour: faint, pleasantly aromatic
Taste: bitter [13].

Geographical source
Native to Central, Eastern, and Southern Europe, this plant is widely grown in North America, the Balkans, Eastern Europe, Germany, and India [14].

Parts used
The flowers and leaves of the plant are the main components of medicinal and commercial importance. Flower extracts and essential oils are used to treat a range of ailments, such as skin diseases [15].

Botanical Description

At the end of each stem is a 5 to 7 cm flower head with narrow sepals covered in glandular hairs. It features orange-yellow tubular florets inside. The disc florets are sterile pseudohermaphrodites, while the female ray florets at the edge are without stamens and have more developed ovaries. Only the female ray florets produce sickle-shaped, curved fruits. Each stem ends with a 5 to 7 cm flower head adorned with narrow sepals covered in glandular hairs. Inside, it has orange-yellow tubular florets. The disc florets are sterile pseudohermaphrodites, whereas the female ray florets at the edges lack stamens and have more developed ovaries. Only these female ray florets produce curved, sickle-shaped fruits [16]. (Fig-1)

[Fig-1 Calendula Flower]

Morphology

C. officinalis Linn. is a plant that can be annual or biennial, growing to a height of 30-60 cm. The lower leaves are spatulate, measuring 10-20 cm in length and 1-4 cm in width, while the upper leaves are oblong and have a mucronate tip, ranging from 4-7 cm long. The stem is angular, hairy, and solid. The flower heads are bright yellow to orange. In cultivated varieties, the marginal flowers are arranged in multiple rows, with oblong spatulate corollas that are 15-25 mm long and 3 mm wide. The corollas of the disc flowers are rounded with a tridentate top, measuring 1.5-2.5 cm in length and 4-7 mm in diameter, and feature 5 mm long tubular florets [17]. C. officinalis has a flower that sits on a clear green base. The middle of the flower is made up of orange-yellow, tube-shaped florets that are often called petals [18].

Various Name of Calendula

Sr.no	Languages	Common Name
1	English	Pot marigold, Scoth Marigold, Calendula, Mary bud, Gold-bloom, Holli gold, English Marigold
2	Hindi	Genda
3	French	Souci des Jardins
4	Spanish	Maravilla, calendula
5	Portuguese	Wonders, boninas
6	Italian	Calendula, florrancio
7	German	Ringelblume.

[Table-1 Various Name of Calendula] [19]

Cosmetic use

Cosmetic ingredients from *Calendula officinalis* (marigold) have various uses and functions, as listed in the International Cosmetic Ingredient Dictionary. Manufacturers report their use of these ingredients through the FDA's voluntary program (VCRP). Data on their concentrations and usage in products are provided, but some specific details, like concentrations in baby lotions, are missing. The CTFA (Cosmetic, Toiletry, and Fragrance Association). survey shows current use concentrations for *Calendula* flower extract and oil. In Europe, *Calendula officinalis* products are used as moisturizers, with no restrictions on their use [20].

Active components are present in *Calendula officials*

The ethanolic extract of Calendula officinalis contained alkaloids, flavonoids, and saponins. The aqueous extract had flavonoids and saponins. Quinone extracts from different parts of the plant provided plastoquinone, phylloquinone, tocopherol, and ubiquinone. Terpenoids were found in the petroleum ether extract of the flowers [21]. phytochemicals analyses have identified a range of chemical compounds such as carbohydrates, amino acids, lipids, carotenoids, terpenoids, flavonoids, essential oils, quinines, coumarins, and other constituents, as detailed in Table [22].

Sr.no	Plant Part	Active Component	Constituents
1	Flower [Fig-2]	Terpenoids	Erythrodiol, Calenduloside, Calendulaglycoside A, Calendulaglycoside B

		Flavonoids	Quercetin, Isorhamnetin, Isoquercitrin, rutin, calendoflavoside
		Coumarin	umbelliferone
		Volatile Oil	Cubenol, α-cadinol, oplopanonec, methyllinoleate
2	Leaves [Fig-3]	Quinones	Phylloquinone,α-tocopherol,ubiquinone, plastoquinone
3	Roots [Fig-4]	Terpenoid	Calenduloside B

[Table-2 Active components are present in Calendula officinalis]

[Fig-2 Calendula Flowers & Leaves]

[Fig-3 Calendula Root]

Taxonomy Classification

Kingdom: Plantae
Order: Asterales
Family: Asteraceae
Tribe: Calendula
Genus: Calendula
Species: officinalis [23].

Chemical Constituents

The Calendula officinalis plant has saponins, triterpeneol esters, and flavonoids. Its orange flowers are full of carotenoids. The leaf extract contains fatty acids, chloroform extracts, triterpenes, and sterols. The water extract has saponins, phenolic compounds, and tannins. The ethanolic extract includes alkaloids, flavonoids, and saponins, while the aqueous extract contains flavonoids and saponins [24].

Pharmacological Activity

I. Anthelmintic effects

The Calendula officinalis plant, which contains saponins, has shown anthelmintic effects, suggesting that saponins contribute to its ability to combat worms [25].

II. Cardiovascular effect

Calendula extract has been shown to decrease the size of myocardial infarctions. It appears to protect the heart by converting signals that normally lead to cell death during ischemia and reperfusion into signals that promote cell survival [26].

III. Anti-Diabetic

The use of Calendula officinalis hydro glycolic extract for treating diabetic foot ulcers (DFUs) was studied, showing no side effects. The results suggest that the extract is safe and helps in healing DFUs. More randomized, controlled trials are needed to confirm its safety and effectiveness for treating DFUs topically [27].

IV. Anti-microbial

The essential oil from the flowers stops the growth of Bacillus subtilis, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, and Candida albicans in the lab. A flavonoid fraction from the flowers also inhibits S. aureus, Sarcina lutea, E. coli, Klebsiella pneumoniae, and Candida monosa. Flower extracts also inhibit Trichomonas vaginalis. Oxygenated terpenes seem to be the key compounds responsible for these antimicrobial effects [28]. Calendula extracts have demonstrated effectiveness against both gram-positive and gram-negative bacteria [29].

V. Wound Healing

Calendula officinalis flower extract helps heal wounds and burns when applied to the skin or taken orally, as indicated by increased hexosamine and collagen-hydroxyproline levels. Marigold extract also protects the skin from UV-B damage. The best way to apply it is through a gel, which maintains reduced glutathione levels and does not impact gelatinase and myeloperoxidase activities affected by UV-B exposure. This gel also lessens skin damage caused by UV-B rays [30].

VI. Antioxidant effects

The leaves and petals of Calendula officinalis might serve as a natural source of antioxidants [31]. The assessment of Calendula officinalis's in vitro antioxidant activity through various methods revealed a dose-dependent response against different radicals· Calendula officinalis extract was tested for antioxidant properties in vitro and in vivo. It effectively scavenged superoxide and hydroxyl radicals, inhibited lipid peroxidation, and neutralized ABTS and DPPH radicals, with IC50 values of 6.5 mg/ml and 100 mg/ml, respectively. The extract also reduced nitric oxide levels with an IC50 of 575 mg/ml and showed dose-dependent activity. It increased catalase activity and glutathione levels in mice, while raising glutathione reductase and lowering glutathione peroxidase levels [32]. An extract of Calendula officinalis was tested for antioxidant effects and found to decrease superoxide production in macrophages of female Swiss albino mice by 12.6% at 100 mg/kg and 38.7% at 250 mg/kg body weight when given orally [33]. C. officinalis exhibits powerful antioxidant properties and can stimulate cellular antioxidants, making it useful for addressing conditions like heart disease, inflammation, and cancer [34].

VII. Hepatoprotective effect

Calendula officinalis extracts were shown to potentially protect the liver from damage and oxidative stress induced by carbon tetrachloride. They also help increase total haemoglobin levels. The extract has a similar consistency to insulin, indicating that it has both antidiabetic and antihyperlipidemic effects [35]. Aflatoxin-related liver toxicity [36].

VIII. Anti-inflammatory

Calendula officinalis is often found in tinctures, ointments, and infusions for wound healing and treating skin issues, including inflammations, blisters, and scars. Research indicates that calendula extract cream can help with burn edema, and its essential oil inhibits various bacteria and fungi in vitro [37]. Calendula officinalis is rich in flavonoids that contribute to its anti-inflammatory effects, alongside potentially significant triterpene saponins and carotenoids [38].

Preparation of Extract

Extraction method 1: To extract and isolate the flowers of Calendula officinalis, we used ethyl alcohol, methyl alcohol, acetone, chloroform, and water. We soaked 4 grams of dried flowers in 100 ml of each solvent for 10-15 days. After soaking, we filtered the solutions with Whatman filter paper No. 1 and tested them using chromatography, spectroscopy, and antimicrobial activity methods

Extraction method 2: The dried flowers of Calendula officinalis L. were ground into fine powder (about 0.3 mm in size). This powder was then soaked in a mixture of 50% ethanol and water (1 part powder to 9 parts liquid) at room temperature (25°C) for 5 days. During this time, the mixture was stirred at 870 rpm for 1 hour at the start and end of the soaking period. After soaking, the mixture was filtered and the liquid was dried at 40°C in an air-circulated oven. The remaining substance was then mixed with 200 mL of a 50% alcohol-water solution and kept in a freezer at −20°C. The final concentrated extract had 15.7% dry weight [39].

Toxicological Studies

The hydroalcoholic extract from Calendula officinalis flowers was tested on rats and mice and didn't show immediate toxicity even at high doses of 5.0 g/kg. There were no changes in blood cell counts at lower doses (0.025, 0.25, 0.5, and 1.0 g/kg). However, higher doses caused an increase in blood urea nitrogen (BUN) and alanine transaminase (ALT), indicating stress on the kidneys and liver [40]. Pregnant women should be cautious with calendula, as it may trigger labor [41].

Traditional Use

The dried flower heads have been utilized for their ability to reduce fever, combat tumors, and promote wound healing [42]. The herb is also employed to heal wounds and address conditions such as measles, smallpox, and jaundice [43]. Calendula tea is utilized for gargling, eye rinses, and addressing issues like conjunctivitis, diaper rashes, haemorrhoids, stomatitis, and mucous membrane inflammation [44]. Dried flowers are used in sweat-inducing, blood-cleansing, blood sugar-lowering, and insect repellent products [45]. Two trials show that various C. officinalis extracts effectively prevent and treat radiodermatitis and radiation-induced oral mucositis in head and neck cancer patients [46]. Calendula is recognized in Ayurvedic and Unani medicine for reducing fever, preventing seizures, and fighting bacteria. It is also used in traditional and homeopathic medicine for vision problems, menstrual issues, varicose veins, haemorrhoids, and ulcers. The plant is noted for treating inflammation, digestive ulcers, and soothing cuts and burns. Calendula officinalis is widely acknowledged for its therapeutic benefits, listed in medical references like the German Commission E and WHO monographs. It is included in products like Caryophyllene ointment, pot marigold tincture and ear drop for treating ear pain in children with infections [47].

Marketed Formulation of *Calendula Officinalis.*

Formulation of Antifungal Gel: To prepare the gel, first disperse the gelling agent in water, stirring at 1200 rpm for 30 minutes. Next, dissolve the drug in a non-aqueous solvent with a preservative, and then add this solution to the

gel while stirring continuously. In Phase A, start by placing water in a beaker and adding Carbopol 940, stirring until it is completely dissolved. Add glycerine and continue stirring, then incorporate propylene glycol (PG), mixing well. Finally, add dimethyl hydantoin (DM DM) while continuing to stir. In Phase B, use another beaker to weigh PEG40 hydrogenated castor oil, and mix in diethylene glycol monoethyl ether until the mixture becomes transparent. Add lavender oil, calendula oil, and vitamin E one at a time, ensuring thorough mixing after each addition Combine Phase B with Phase A and mix thoroughly. Check the pH of the mixture and adjust it with triethanolamine if necessary. The result should be a clear, transparent gel [48].

Formulation of Marigold cream: An oil-in-water (O/W) emulsion cream was prepared by heating stearic acid, olive oil, and acetyl alcohol with flower extract to 75 °C. Separately, preservatives and water-soluble components were heated, then gradually mixed into the oil phase while stirring until a cream formed, which was then cooled at room temperature [49].

Formulation available in market:

Sr.no	Product Name	Company name	Use
1	Calendula Scalp Serum	THE LIVING CO.	Hair straightening & Smoothening.
2	Calendula Lotion	CALENDULA Plus	For dry & itchy skin.
3	Organic baby massage oil	juicy chemistry Junior Care	Smooth $ moisturiser baby scalp $ body.
4	Acne pimples face pack	Arogyam ayurveda	Foe acne pimples, minimize pores.

[Table-3 Marketed formula]

Future Perspectives:

Calendula officinalis has been used for centuries for its health benefits. It contains various compounds, such as terpenoids, steroids, phenolic substances, carotenes, and essential oils, with cadinol being a key component. These compounds give Calendula officinalis its wide range of benefits, including reducing inflammation, diabetes management, antioxidant effects, cancer prevention, and more. Future research should explore the non-floral parts of Calendula officinalis (like seeds, roots, leaves, and stems) and other Calendula species to better understand their properties. It's also important to study how different plant ages, extraction methods, and processing affect its benefits. As extraction techniques improve, new beneficial compounds and uses for Calendula officinalis may be discovered. Research into new ways to deliver Calendula officinalis in medicines is still ongoing, and advanced techniques like molecular docking and bioinformatics are promising for finding new treatments [50].

Conclusion

Calendula officinalis is a multifaceted herb with a long-standing history in herbal medicine, known for its anti-inflammatory, antimicrobial, antioxidant, and wound-healing properties. Its bioactive compounds, including flavonoids, terpenoids, and saponins, contribute significantly to its therapeutic potential, making it applicable in managing conditions such as diabetes and cardiovascular diseases. Traditional uses have been substantiated by modern research, highlighting the herb's safety and minimal toxicity, which supports its inclusion in various herbal formulations. Future studies should delve deeper into the less-explored parts of the plant and advanced extraction methods to fully realize the ultimate therapeutic benefits of this versatile herb.

REFRENCE:

1. Shahane K, Kshirsagar M, Tambe S, Jain D, Rout S, Ferreira MK, Mali S, Amin P, Srivastav PP, Cruz J, Lima RR. An updated review on the multifaceted therapeutic potential of Calendula officinalis L. *Pharmaceuticals*. **2023;**16(4):2-21.
2. Duda MM, Bunescu H, Fiţiu A, Vaida S. Research on the cultivation of 8 marigold varieties (Calendula officinalis L.) in various conditions of fertilization in the Jucu. Cluj. *Bulletin UASVM Agriculture*.**2010**;67(1):2-7.
3. Baciu AD, Mihalte L, Sestras AF, Sestras RE. Variability of decorative traits, response to the Aphis fabae attack and RAPD diversity in different genotypes of Calendula. *Notulae Botanicae Horti Agrobotanici Cluj-Napoca*. **2010;**38(3):265-70.
4. Ullah MA, Hassan A, Hamza A. Calendula (Calendula officinalis) marigold as medicinal plant. *Orthopaedics Case Rep*. **2023;**2(1):1-9.
5. Silva D, Ferreira MS, Sousa-Lobo JM, Cruz MT, Almeida IF. Anti-inflammatory activity of Calendula officinalis L. flower extract. *Cosmetics*. **2021**;8(2):31.
6. Dhingra G, Dhakad P, Tanwar S. Review on phytochemical constituents and pharmacological activities of plant Calendula officinalis Linn. *Biological Sciences*. **2022**;2(2):216-28./

7. Ahmad S, Ahmed W, Mihoub A, Jamal A, Farhan Saeed M, Masood N, Radicetti E, Fawad M, Nicola S. Developmental, Phytochemical and Enzymatic Changes in Pot Marigold (Calendula officinalis L.) cvs. Hybrid and French with Salicylic Acid (SA) and Polyamine Spermidine (SP) Foliar Spray. *Agronomy.* **2023**;13(1):191.
8. Kumar N, Sharma J, Sharma S. Pharmacognostical and phytochemical investigation of Calendula officinalis. *Journal of Advanced Scientific Research*. **2010**;1(01):61-6.
9. Chakraborthy GS. Phytochemical screening of Calendula officinalis Linn leaf extract by TLC. *Internsational journal of research and ayurveda and pharmacy*. **2010** ;1(1) 131-134.
10. Akhtar N, Zaman SU, Khan BA, Haji M, Khan S, Ahmad M, Rasool F, Mahmood T, Rasul A. Evaluation of various functional skin parameters using a topical cream of Calendula officinalis extract. *African journal of Pharmacy and Pharmacology*. **2011**;5(2):199-206.
11. Bernatoniene J, Masteikova R, Davalgiene J, Peciura R, Gauryliene R, Bernatoniene R, Majiene D, Lazauskas R, Civinskiene G, Velziene S, Muselik J. Topical application of Calendula officinalis (L.): Formulation and evaluation of hydrophilic cream with antioxidant activity. *Journal of Medicinal Plants Research*. **2011** ;5(6):88-77.
12. Jodh R, Tawar M, Behere S, Randhave N, Jirapure P, Ingle S. A review on Calendula officinalis*. Research Journal of Pharmacognosy and Phytochemistry*. **2023;**15(1):5-10.
13. Singh MK, Sahu P, Nagori K, Dewangan D, Kumar T, Alexander A, Badwaik H, Tripathi DK. Organoleptic properties in-vitro and in-vivo pharmacological activities of Calendula officinalis Linn: An over review. *J Chem Pharm Res.* **2011**:3(4):655-63.
14. Khan MU, Rohilla A, Bhatt D, Afrin S, Rohilla S, Ansari SH. Diverse belongings of Calendula officinalis: an overview. *Int J Pharm Sci Drug Res*. **2011**;3(3):173-7.
15. Priyanka Mishra PM, Patidar A, Gupta D, Agrawal S. Treatment of acne with herbal remedie-Calendula officinalis: an overview. *International journal of Pharmaceutics &Biological Archives*.**2011**;2(4):1020-1023.
16. Muley BP, Khadabadi SS, Banarase NB. Phytochemical constituents and pharmacological activities of Calendula officinalis Linn (Asteraceae): a review. *Tropical journal of pharmaceutical research*. **2009;**8(5).455-465.
17. Arora D, Rani A, Sharma A. A review on phytochemistry and ethnopharmacological aspects of genus Calendula. *Pharmacognosy reviews*. **2013**;7(14):179-187.
18. Safdar W, Majeed H, Naveed I, Kayani WK, Ahmed H, Hussain S, Kamal A. Pharmacognostical study of the medicinal plant Calendula officinalis L.(family Compositae). *Int J Cell Mol Biol*. **2010**;1(2):108-16.
19. B Sapkota , Kunwar P. A Review on Traditional Uses, Phytochemistry and Pharmacological Activities of Calendula officinalis Linn. *Natural Product Communications*. **2024**;19(6):2-22.
20. 20)Andersen FA, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, Liebler DC, Marks JG, Shank RC, Slaga TJ, Snyder PW. Final report of the Cosmetic Ingredient Review expert panel amended safety assessment of Calendula officinalis—derived cosmetic ingredients. *International journal of toxicology*. **2010**;29(4):221-243.
21. Pintea A. HPLC analysis of carotenoids in four varieties of Calendula officinalis L. flowers. *Acta Biologica Szegediensis.* **2003** ;47(1-4):37-40.
22. Jan N, John R. Calendula officinalis-an important medicinal plant with potential biological properties. *Proc Indian Natn Sci Acad* **2017**, 769-787.
23. Mishra AK.et al.; calendula officinalis: an important herb with valuable Therapeutic dimensions -an overview: *journal of global pharma technology*; **2010**; 2(10): 14-23.
24. Patil K, Sanjay CJ, DoggALLI N, Devi KR, Harshitha N. A Review of Calendula OfficinalisMagic in Science*. Journal of Clinical and Diagnostic Research*. **2022**;16(2): 23-7.
25. Lipi Purwal LP, Vivek Shrivastava VS, Makode KK, Jain UK. Anthelmintic activity of aqueous extracts of some saponin containing medicinal plants. *Der Pharmacia Lettre.* **2010**;2(4):476-81.
26. Kumar N, Sharma J, Sharma S. Pharmacognostical and phytochemical investigation of Calendula officinalis. *Journal of Advanced Scientific Research*. **2010**;1(01):61-6.
27. Miraj S. The role of medicinal plants in the treatment of diseases: A systematic review of Calendula officinalis*. Der Pharmacia Lettre.* **2016**;8(14):92-5.
28. Baskaran K, Marigold C, Marigold G, English PM, German B. Pharmacological activities of Calendula officinalis. *Int. J. Sci. Res.* **2017**;6(5):43-7.
29. Ejiohuo O, Folami S, Maigoro AY. Calendula in modern medicine: Advancements in wound healing and drug delivery applications. *European Journal of Medicinal Chemistry Reports.* **2024;**1-14.
30. Sharma S, Kumari K. An overview on Calendula officinalis Linn.:(pot marigold). *Journal of Advanced Scientific Research*. **2021**;12(3):13-8.
31. Preethi KC, Kuttan G, Kuttan R. Antioxidant Potential of an Extract of Calendula officinalis. Flowers in Vitro. and in Vivo. Pharmaceutical biology. 2006 Jan 1;44(9):691-7.
32. Al-Snafi AE. The chemical constituents and pharmacological effects of Calendula officinalis-A review. *Indian Journal of Pharmaceutical Science & Research.* **2015**;5(3):172-85.
33. Ashwlayan VD KA, Verma M. Therapeutic potential of Calendula officinalis. *Pharm Pharmacol Int J.* **2018**;6(2):149-55.
34. Nagaraj NJ, Ravikumar N, Mahalaxmi S, Pallavi S. Effect of Calendula officinalis Linn in Oral health- A Review. *International Journal of Ayurvedic Medicine.* **2022**;13(3); 601-605.

35. Manal, Sh.Hussein, Osama, S.El-Tawil,A. Abdou. Tetrachloride-Induced PE, In H. The protective effect of Morus alba and Calendula officinalis plant extracts on carbon tetrachloride-induced hepatotoxicity in isolated rat hepatocytes. *Journal of American Science.* **2010**;6(10):762-773.
36. Hamzawy MA, El-Denshary ES, Hassan NS, Mannaa FA, Abdel-Wahhab MA. Dietary Supplementation of Calendula officinalis Counteracts the Oxidative Stress and Liver Damage Resulted from Aflatoxin. *ISRN Nutr*. **2013**:1-9.
37. Lalit A, Palve L, Shendkar M, Bhosle M, Parkhi L, Kothavle S, Jagtap K. The Science and Tradition of Calendula: A Review of Phytochemistry and Ethnopharmacology. *Navsahyadri institute of pharmacy, Nasarapur, Pune-412213, India*. **2024**;2(7):2033-2040.
38. Shafeie N, Naini AT, Jahromi HK. Comparison of different concentrations of Calendula officinalis gel on cutaneous wound healing. *Biomedical and Pharmacology Journal.* **2015**;8(2):979-92.
39. Fonseca YM, Catini CD, Vicentini FT, Nomizo A, Gerlach RF, Fonseca MJ. Protective effect of Calendula officinalis extract against UVB-induced oxidative stress in skin: Evaluation of reduced glutathione levels and matrix metalloproteinase secretion. *Journal of ethnopharmacology*. **2010**;127(3):596-601.
40. Khalid KA, da Silva JT. Biology of Calendula officinalis Linn.: focus on pharmacology, biological activities and agronomic practices*. Medicinal and Aromatic Plant Science and Biotechnology.* **2012**;6(1):12-27.
41. Verma PK, Raina R, Agarwal S, Kaur H. Phytochemical ingredients and Pharmacological potential of Calendula officinalis Linn. *Pharmaceutical and Biomedical Research*. **2018** 10;4(2):1-7.
42. Ukiya M, Akihisa T, Yasukawa K, Tokuda H, Suzuki T, Kimura Y. Anti-inflammatory, anti-tumor-promoting,and cytotoxic activities of constituents of marigold flower. *J Nat Prod.***2006;**69(12):1692-6.
43. Matysik G, Wójciak-Kosior M, Paduch R. The influence of Calendulae officinalis flos extracts on cell cultures, and the chromatographic analysis of extracts. *J Pharm Biomed Anal*. **2005**;38(2):285-292.
44. Mozherenkov VP, Shubina LF. Treatment of chronic conjunctivitis with Calendula. *Med Sestra*. **1976**;35(4):33-34.
45. Chaparzadeh N, D'Amico ML, Khavari-Nejad RA, Izzo R, Navari-Izzo F. Antioxidative responses of Calendula officinalis under salinity conditions. *PlantPhysiol Biochem.***2004**;42(9):695-701.
46. Cruceriu D, Balacescu O, Rakosy E. Calendula officinalis: potential roles in cancer treatment and palliative care. *Integrative cancer therapies*. **2018**;17(4):1068-78.
47. Abdelwahab SI, Taha MM, Taha SM, Alsayegh AA. Fifty-year of global research in Calendula officinalis L.(1971–2021): A bibliometric study. *Clinical Complementary Medicine and Pharmacology*. **2022**;2(4):2-10.
48. Archi D, Pooja K, Shital F. Formulation and Evaluation of Calendula and Lavender Oil Based Topical Antifungal Gel. *Journal of Pharmaceutical Research International***. 2024** ;36(7):133-47.
49. Alsaraf KM, Abbas IS, Hassan EF. Extraction and clinical application of Calendula officinalis L. flowers cream. *InIOP Conference Series: Materials Science and Engineering* **2019**; 571;1-11.
50. Mali SN, Tambe S, Pratap AP, Cruz JN. Molecular modeling approaches to investigate essential oils (volatile compounds) interacting with molecular targets. *InEssential Oils: Applications and Trends in Food Science and Technology* **2022;** 417-442.