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Formulation of Topical Gel Using Cissus Quadrangularis Plant Extract- An In Vitro Study

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ABSTRACT:

Plants have been used by humans as a natural source of remedies and cures since ancient times. Medicinal herbs have gained popularity due to their widespread application and low toxicity. Perennial climber *C.quadrangularis* is widely utilized in Indian traditional medicine systems. It has been shown to have analgesic, antibacterial, antifungal, antioxidant, anthelmintic, and bone fracture healing effects. The analgesic properties of this plant extracts are mostly beneficial for arthritis, and bone repair which helps in improving people's comfort and promoting mobility. The study aimed to assess the anti-inflammatory property of *C.quadrangularis*. The microbial activity of the *C.quadrangularis* plant extract was prepared using different solvents such as ethanol, methanol, DMSO, chloroform, ethyl acetate. The antimicrobial activity of the plant extract was analyzed against both gram-positive and gram-negative bacteria namely *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus,Bacillus subtilis, Klebsiella pneumoniae, Proteus mirabilis* by agar well diffusion method. They reveal a significant zone of inhibition against *Bacillus subtilis*. The preliminary phytochemical screening of the plant extract was performed to identify the compounds such as flavonoids, tannins, terpenoids, saponin, and steroids. The topical formulation was prepared using a methanolic extract of *C.quadrangularis*. The in vitro study of *C.quadrangularis* infused topical gel using the HET-CAM method shows that haemorrhage was not observed. The resulting formulated topical gel had antibacterial, antifungal, analgesic and anti-inflammatory effects and it is also safe and eco-friendly.

1. Introduction

Natural materials have been employed, either directly or indirectly, as the primary source of medicines for many years, and their health benefits to humans have been demonstrated without question (Piyush *et al.,* 2021). A remarkable number of modern medications have been discovered from natural sources, with many originating from their use in traditional medicine (K.F. Chah et al., 2006). Plants, animals, and humans are treated for a variety of diseases with the help of extracts and infusion components made from medicinal plant parts such as leaves, seeds, stems, roots, fruits, foliage, etc., (Anibijuwon *et al.,*2009). Every species generates a variety of bioactive substances or secondary metabolites (Anandaramajayan *et al.,* 2019).

Many compounds from plants used in traditional medicine have the potential to treat both viral and chronic diseases (Duraipandiyan et al., 2006). Thousands of phytochemicals derived from plants were discovered to be safe, generally efficient substitutes with fewer side effects. Advantageous biological properties, including antibacterial, antioxidant, anticancer, antidiarrheal, analgesic, and wound healing properties, have been documented (Sasidharan *et al.,* 2011). Therefore, substances obtained from therapeutic plants are regarded as a primary source of pharmaceuticals and are presumed to be safe. The bulk of medications were formerly made from naturally occurring microbiological sources, but herbal medicine has become moreand more well-liked as an alternative to regular medical care (Koduru *et al.,*2006).

C.quadrangularis, also referred to as Hadjod is a perennial plant that belongs to the Vitaceae family. Other names for it are devil's backbone, square stalked vine, veldt grape, asthisamharaka, hadjod and pirandai, Sannalam, Nalleru, Vajravelli, and Mangara valli. It is indigenous to Bangladesh, Sri Lanka, and India (Ayesha *et al.,* 2017). The plant is abundant in vitamin C, beta-carotene, and anabolic steroids. Its alcoholic extract has been shown to accelerate recovery from bone fractures in rats (Singh *et al*). Traditionally, this herb has been utilized as an analgesic, digestive tonic, anthelmintic, antidyspeptic, and for the treatment of asthma and scurvy (Chidhambaram Murthy *et al*., 2003). It has also been reported to have various medicinal applications for gout, piles, tumors, peptic ulcers, and leucorrhoea (Nagani *et al*., 2011). Key constituents of

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the plant include iridoids such as 6-O-meta-methoxy-benzozyl catapol, picroside, and pallidol; phytosterols like β-sitosterol and calcium; flavonoids such as quercetin, daidzein, and genistein; triterpenoids like friedelin; and Stilbene derivatives, including quadrangularin-A, resveratrol, and piceatannol (Prasad *et al*., 1963; Day *et al*., 2003). The stem sections contain calcium oxalate, vitamin A, β-amyrins, β-sitosterol, ketosetosterol, phenols, tannins, calcium ions, phosphorus, and 31-methyl-tritiacontanoic acid. The aerial parts include a novel asymmetric tetracyclic triterpenoid, 7-Oxo-Onocer-8-ene-3 β 21-α diol. The leaves are rich in resveratrol, piceatanon, pallidol, parthenoxy, and alicyclic lipids. The root powder supplies a range of minerals, including potassium (67.5 mg), calcium (39.5 mg), zinc (3.0 mg), sodium (22.5 mg), iron (7.5 mg), lead (3.5 mg), cadmium (0.25 mg), copper (0.5 mg), and magnesium (1.15 mg) (Jainu *et al*., 2006; Sen *et al*., 2019).

This study describes the medicinal plants and their parts that are employed in the efficient treatment of inflammation and the illnesses that are linked to it. Inflammation is a condition that is linked to many disease states (Pravin *et al.,* 2011). Due to improved tolerance and a decrease in adverse medication reactions, non-synthetic, natural products originating from plant or herbal sources are currently gaining more attention worldwide (Choudhary *et al.,*).

Rheumatoid arthritis is among the most prevalent chronic inflammatory disorders impacting individuals globally. While there are a number of medications that are known to treat these kinds of diseases, extended usage should be avoided because of a number of negative consequences. As a result, novel anti-inflammatory medications with few adverse effects must be developed. Therefore, the current study evaluated the pharmacological potency, safety, and physical properties of a topical gel containing *C.quadrangularis* extract utilizing excipients, as well as setting up standards for the final medical product (Salunkhe *et al.,* 2013).

The word "gel" often refers to highly hydrated networks with two constituents in different proportions: the solvent, which is mostly composed of mass, and the polymeric solute, which is usually composed of either natural or artificial macromolecules. The macromolecule in question needs to be able to hold onto a sizable amount of solvent (Sacco *et al.,* 2018). The use of gel is widespread and growing, especially in the biomedical sector. (Jiang *et al*., 2014).

Natural and synthetic polymers can be used to create hydrogels. However, synthetic polymers are used more often than natural ones. Because of its exceptional physical and rheological qualities, carbomer (carbopol) is the most widely used synthetic polymer among others. Furthermore, there have been no reports of skin irritation or lipid vesicle stability issues with carbopol. Numerous investigations have effectively demonstrated carbopol's efficacy as a transdermal lipid vesicle carrier. Furthermore, liposomes have been successfully transported from the carbopol to the deeper skin according to research using electron paramagnetic resonance (Shashank *et al.,* 2016).

Hen's Egg test on chorioallantoic membrane (HET-CAM) analysis is a novel, well- liked, and alternative method for animal experiments that will be used to evaluate the anti-inflammatory efficacy of the ideal formulation that has been chosen (Ozturk *et al.,* 2020). This study aims to create a topical gel for anti-inflammatory using herbal plant *C.quadrangularis*. The resulting formulated gel had great antibacterial, antifungal, analgesic, and anti-inflammatory effects and it is also safe, non-toxic, and eco-friendly.

2. Materials and Methods

Collection of *C. quadrangularis* plants:

Fresh *C. quadrangularis* plants were obtained from a local market, chopped into small pieces, and dried in the shade for three to four weeks. Post-drying, the plants were ground into a fine powder for further use.

Solvent extraction of C.quadrangularis plant: (Anitha *et al.*, 2010)

Solvent extraction of the plant was performed using ethanol, methanol, chloroform, ethyl acetate, and DMSO. Five grams of the extract were dissolved in 50 ml of solvent, filtered through Whatman No. 1 paper, and evaporated to dryness. The dried extract was weighed and dissolved in DMSO for further research.

Test organisms:

The extract's antimicrobial properties were tested on various bacteria (e.g., *Klebsiella, E. coli*) and fungi (e.g., *Aspergillus niger*).

Antimicrobial activity:

Agar well diffusion: (Murthy *et al.*, 2003)

The antibacterial activity of different extracts was assessed using the agar well diffusion method (Murthy *et al*., 2003). Cultures were swabbed on agar, and 50 µl of solvents (ethyl acetate, methanol, chloroform, ethanol, DMSO) were added to wells. Inhibition zones were measured after 24-72 hours at 37°C.

Antifungal activity: (Selvaraj *et al.*, 2010)

The antifungal activity was evaluated by immersing sterile discs in various extracts soaked in 1 ml of DMSO, which were then dried at 40°C for 30 minutes. Sabouraud dextrose agar (SDA) medium used to asses antifungal activity . Inhibition zones were measured after 72 hours at 25°C.

Minimum Inhibitory Concentration: (Nigussie *et al.*, 2021)

The Minimum Inhibitory Concentration (MIC) is the lowest antibiotic concentration preventing visible bacterial growth after overnight incubation. Determined by microscopic analysis, MIC uses 12 sterilised test tubes with LB broth, where varying extract concentrations (10 µl-100 µl) were added to 10 tubes. Absence of turbidity indicated the MIC, confirming no bacterial growth.

Phytochemical screening: (Doss *et al.*, 2009)

The crude extract *of Cissus quadrangularis* underwent preliminary phytochemical screening to identify various compounds.

Chemical characterization of extract using FTIR: (Alizadeh-Sani *et al.*, 2021)

The chemical bond and functional group of the film were obtained using a fourier transform infrared (FTIR) spectrometer (Thermo fisher scientific) at the range of 300-3500 cm−1.

Formulation of hydrogel using Carbopal Formulation of gel:(Teradale *et al* , 2022)

Gels were prepared by dissolving methylparaben in purified water at 40°C using carbopol-940, and the mixture was stirred at 1200 rpm for 30 minutes. The *C. quadrangularis* extract, dissolved in ethanol and propylene glycol, was gradually added to the polymeric solution. Tri-ethanolamine adjusted the gel's pH (Teradale et al., 2022).

The evaluation of a formulated gel involved several tests (Sarkar *et al.*, 2016):

Physical Evaluation:

The physical evaluation was Observed by colour and appearance of the herbal gel formulations.

pH Measurement:

The pH of the gel was determined using digital pH meter by dissolving the gel in water and recording the reading with a glass electrode.

Spreadability:

Spreadability was Measured using a wooden block and weight; calculated spreadability with the formula

$$S = M \times L / T,$$

where S is Spreadability, M is the weight, L is the distance moved, and T is the time.

Homogeneity:

Homogeneity was Visually inspected for uniformity, appearance, and absence of aggregates.

Evaluation of Anti-Inflammatory activity of synthesised hydrogel by an in-vitro assay(HET-CAM method): (Ismailovi *et al.*,2024)

Fertilised hen eggs were rotated several times and incubated for 72 hours at 36.5°C and 80% humidity. Albumin was extracted, shells removed, and cavities covered with film for another 72 hours. On day six, test treatments on CAMs reduced SDS-induced granulomas, normalising membrane irritation.

3. Result

Antimicrobial assessment of *C.quadrangularis* plant extract.

Antibacterial activity of plant extract:

C. quadrangularis powder was tested for antimicrobial activity using different solvents (ethanol, methanol, ethyl acetate, DMSO, chloroform) via well diffusion method. The methanolic extract exhibited the highest antibacterial activity, showing inhibition zones against Proteus mirabilis (15mm), *Bacillus subtilis* (13mm),*Pseudomonas aeruginosa* (10mm), *Escherichia coli* (10mm), *Klebsiella pneumoniae* (10mm), and *Staphylococcus aureus*(4mm)**(Fig 1)**

Antifungal activity:

Penicillium sp., Candida albicans, Aspergillus flavus, and Aspergillus niger were tested for antifungal activity, methanol, ethyl acetate, chloroform, and ethanol extract of *C.quadrangularis* showed 16mm, 12mm, 11mm, and 10mm respectively against *Penicillium sp.* **(Fig 2)** and **(Table 1).**

Minimum Inhibitory Concentration:

The MIC of *C. quadrangularis* extract, ranging from 50µg to 100µg, effectively inhibited P. mirabilis, B. subtilis, K. pneumoniae, E. coli, S. aureus, and P. aeruginosa**(Table 2).**

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Phytochemical Screening of C.quadrangularis extract:

Phytochemical analysis of *C.quadrangularis* extract indicated the presence of terpenoids, tannins, glycosides, alkaloids, flavonoids, quinones, and saponins**(Table 3).**

Fourier Transform Infrared Spectroscopy:

The gel's structure is defined by molecular interactions like covalent and hydrogen bonds. FT-IR analysis (500 cm^{-1} - 3500 cm^{-1}) revealed complex vibrational modes, e.g., 602.40 cm^{-1} and 3328.32 cm^{-1} **(Fig 4)** and **(Table 4).**

Evaluation of C.quadrangularis infused Gel:

The herbal gel formulations demonstrated characteristic colour and appearance, had an optimum skin pH, a spreadability of 22.73 g.cm/sec, and were visually confirmed to be uniform and homogenous.

HET CAM assay (Anti-Inflammatory):

The initial irritation scores for CAM test samples used NaCl (positive) and NaOH (negative) controls. Haemorrhage analysis showed no end points, yielding a score of 0 for test and negative samples Direct examination of CAM impregnated with extract infused topical gel. The haemorrhage (blood from a ruptured vessel). Hence, the samples treated with plant extract were considered to be biocompatible for the human application **(Fig 3).**

4. Discussion

The medicinal properties of plants are increasingly recognized in pharmaceuticals for their safety and minimal side effects (Verpoorte *et al*., 2012). Rising antibiotic resistance has led to more research (Vashishtha *et al*., 2010). Studies on *Cissus quadrangularis* extracts show methanol's strong antibacterial and antifungal effects, especially against *Bacillus subtilis* and *Penicillium sp*. (Charumathi *et al.*, 2010). Phytochemical screening reveals bioactive compounds, enhancing antibacterial and antifungal properties, and phenolic compounds offering benefits for hyperglycemia, antioxidants, anticancer, and anti-inflammatory treatments.

Fig 1: Antibacterial avtivity of plant extract:

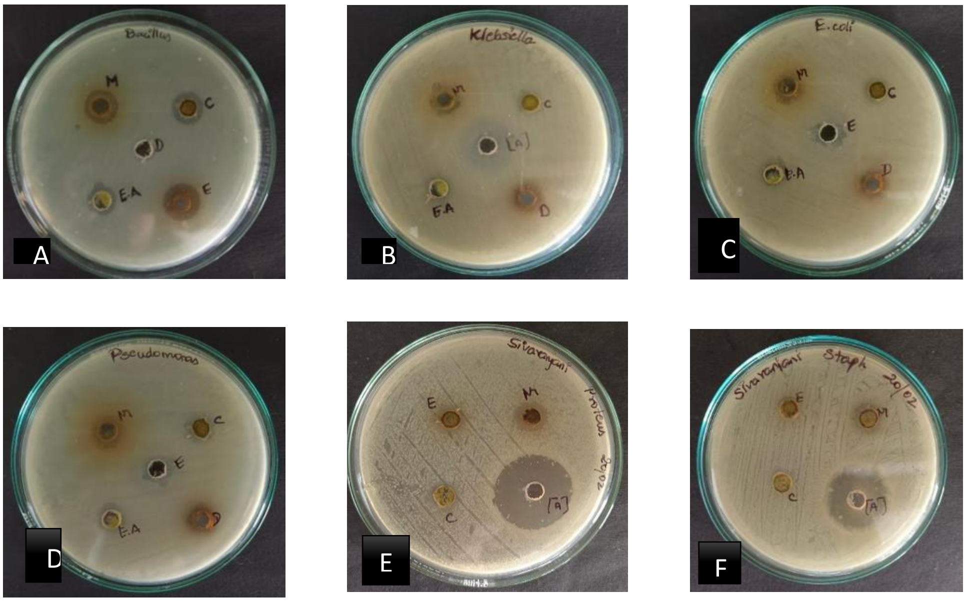

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Fig 2: Antifungal activity:

Fig 3: Assessment of anti-inflammatory activity:

Positive control SDS-1%

Solvent control (H2O)

Negative article (Nacl-0.9%W/V)

Test compound

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Fig 4: FTIR-Spectra for *C.quadrangularis* plant extract

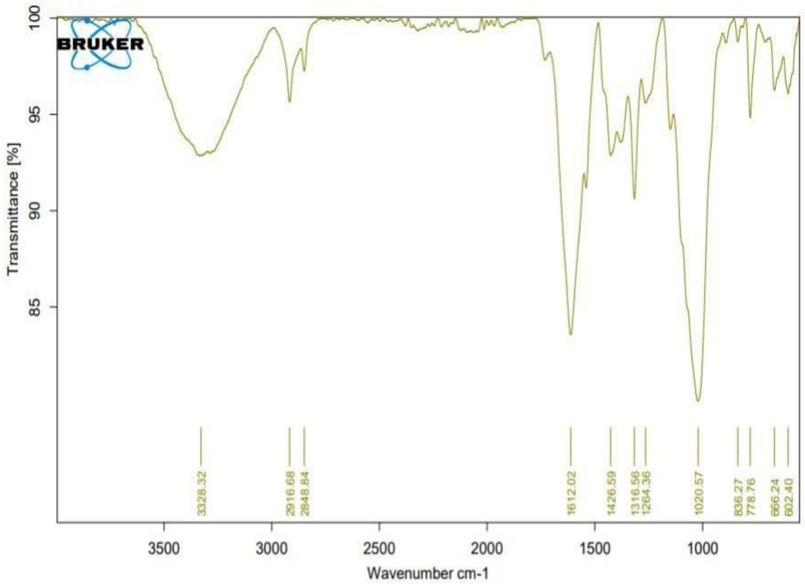

Table 1. Antifungal activity of*C.quadrangularis* extract:

Organism	Ethanol	Ethyl acetate	Methanol	Chloroform
Penicillium sp	10mm	12mm	16mm	11mm

Table 2. Minimum Inhibitory Concentration (MIC) of Methanol Extract of Plant:

Organism	60µl	70µl	80µl	90µl	100µl
P.mirabilis	0.31µl	0.29µl	0.27µl	0.26µl	0.24µl
B.subtilis	0.61µl	0.60µl	0.60µl	0.59µl	0.58µl
K.pneumoniae	0.40µl	0.37µl	0.33µl	0.32µl	0.28µl
P.aeruginosa	0.30µl	0.28µl	0.25µl	0.24µl	0.19µl
E.coli	0.60µl	0.60µl	0.59µl	0.58µl	0.58µl
S.aureus	0.56µl	0.56µl	0.55µl	0.58µl	0.57µl

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Table 3. Phytochemical screening for *C.quadrangularis* plant extract:

S.NO	PHYTOCHEMICAL	PLANT EXTRACT
1.	Alkaloids	+
2.	Flavonoids	-
3.	Terpenoids	-
4.	Tannins	+
5.	Saponins	+
6.	Glycosid	+
7.	Quinine	+

Table 4. FTIR analysis for the *C.quadrangularis* plant extract:

S.No	Frequency (cm-1)	Bond	Functional Group
1	602.40 cm-1	C–Br stretch	Alkyl halides
2	666.24 cm-1	–C≡C–H: C–H bend	Alkynes
3	778.76 cm-1	C–Cl stretch	Alkyl halides
4	836.27 cm-1	C–H “oop”	Aromatics
5	1020.57 cm-1	C–N stretch	Aromatic amines
6	1316.56 cm-1	N–O symmetric stretch	Nitro compounds
7	1426.59 cm-1	C–C stretch (in–ring)	Aromatics
8	1612.02 cm-1	N–H bend	1° amine
9	2848.84 cm-1	H–C=O: C–H stretch	Aldehydes
10	2916.68 cm-1	H–C=O: C–H stretch	Alkanes
11	3328.32 cm-1	N–H stretch	1°, 2° amines, amides

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5. CONCLUSION:

The *C.quadrangularis* plant was extracted using various solvents and tested for antimicrobial activities against bacteria (*P. aeruginosa*, *S. aureus*, *K. pneumoniae*, *P. mirabilis*, *E. coli*, and *B. subtilis*) and fungi (*Penicillium sp*, *Candida albicans*, *Aspergillus* , and *Aspergillus niger*), showing significant inhibition. Methanolic extract analysis revealed compounds like terpenoids and alkaloids. FTIR spectroscopy identified functional groups, and a topical gel was formulated with Carbopol, assessed for various properties and anti-inflammatory efficacy via HET-CAM assay. This study underscores the plant's potential in pharmaceuticals and cosmeceuticals.

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