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Ginseng Extract- Enriched Topical Gel : Design , Characterization and Efficacy in Preventing Epidermiod Carcinoma

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Abstract: *Background: The aim of the present study is to formulate and characterize a Ginseng Extract-loaded topical gel using Carbopol-940 for the treatment of epidermoid carcinoma. The optimized herbal gel formulations were assessed for homogeneity, appearance, pH, viscosity, extrudability, spreadability.*
Results: Formulations F1 to F5 exhibited excellent homogeneity, with pH values ranging from 6.62 to 6.94. Spreadability was observed between 15.70 and 24.37 gm.cm/s, and extrudability ranged from 85.51% to 90.45% w/w.
Conclusion: Topical delivery of Ginseng Extract-Enriched Topical Gelalleviates the side effects caused by systemic chemotherapy; hence, thedeveloped herbal gel formulation can be effectively useful to deliver Ginseng Extract-Enriched Topical Gel in the treatment of epidermoidcarcinoma..

Keywords: Skin cancer, Ginseng, Diffusion, gel, Drug content

I. INTRODUCTION

Cancer is a leading cause of morbidity and mortality globally, ranking as the second most common cause of death worldwide, following cardiovascular diseases[1]. In 2020, around 20 million new cancer cases were diagnosed. Among men, the most prevalent cancers are lung, prostate, stomach, liver, and colorectal, while in women, breast, lung, colorectal, thyroid, and cervical cancers are most common[2]. Patients affected by these cancers urgently need an effective therapy that offers a complete cure[3].Current cancer treatments, such as chemotherapy, surgery, and radiation therapy, often come with serious adverse effects. Since ancient times, natural and herbal medicines have been used to treat and prevent various types of cancer[4].Epidermoid carcinoma, commonly known as skin cancer, is one of the most prevalent cancer types, characterized by the uncontrolled growth of skin cells. It is often triggered by ultraviolet radiation from sunlight or tanning beds, leading skin cells to multiply excessively and form malignant tumors[5].A persistent sore that does not heal within two weeks and noticeable changes in skin appearance are key indicators of skin cancer. Each year, an estimated 2–3 million new cases are diagnosed, with numbers steadily rising. In the northern United States, nearly half of individuals who live to age 65 are expected to develop skin cancer at least once, underscoring a significant and growing public health concern[6].In recent years, the use of herbal medicines and their active constituents for cancer treatment has significantly increased, primarily due to their lower side effects compared to conventional therapies[7]. Phytoconstituents found in herbal medicines have gained prominence in cancer treatment due to their ability to target multiple molecular pathways. Herbal drugs contain a variety of phytoconstituents, such as alkaloids, glycosides, and tannins, which exhibit diverse pharmacological activities. In addition to these active compounds, plants also provide essential vitamins, minerals, proteins, and other beneficial nutrients[8].

Ginseng refers to the root of several species within the plant genus Panax, with Panax ginseng being the most commonly used species, native to Far East countries, particularly China and Korea. The genus name "Panax," given by Russian botanist C.A. Meyer, originates from the Greek words "pan" (meaning "all") and "axos" (meaning "cure")[9]. Ginseng contains multiple chemically active ingredients thatexert positive pharmacological effects, including anti-diabetic[10], anti-inflammation and antioxidative stress, lowering- lipid levels[11], antitumor[12]and cardioprotective effects etc. In addition, it has been noted that the dailyconsumption of ginseng could enhance human physical performance as well as quality of life (QoL)[13]. Panax ginseng exhibits a broad range of pharmacological activities

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against cancer, primarily due to its active compounds such as Compound K and Ginsenosides Rh1, Rh2, Rh3, and F1, which have shown effectiveness in five major cancers: lung, breast, colon, prostate, and stomach cancer[14].The anti-cancer effects of Panax ginseng (PG) and its metabolites operate through three primary mechanisms. First, they inhibit tumor growth by suppressing cell proliferation and inducing apoptosis, primarily via intrinsic apoptosis pathways regulated by Bcl-2, Bax, and Caspase-9, with additional apoptosis effects through pathways like STAT3, NF-kB, MAPK, and Akt. Notably, PGE, G-Rh1, and CK induce cell cycle arrest in colon cancer, with G-Rh2 similarly affecting gastric cancer. Second, PG compounds inhibit tumor progression by repressing epithelial-mesenchymal transition (EMT) in colon and breast cancers and reduce angiogenesis in prostate cancer, targeting multiple factors to help overcome treatment resistance and recurrence. Lastly, PG metabolites combat multi-drug resistance (MDR), as G-Rh2 reduces MDR in breast and colon cancers, while CK enhances cisplatin sensitivity. These findings indicate that ginsenoside metabolites not only hold promise as anti-cancer agents but also as MDR modulators[15-17].To date, no studies have explored the anticancer effects of Ginseng Extract on skin cancer. Conventional treatments for melanoma, including chemotherapy and immunotherapy, often cause side effects such as anorexia, nausea, fatigue, vomiting, renal toxicity, and dermatitis[18]. In contrast, topical herbal gel formulations offer a painless, targeted application with fewer side effects, making them effective for skin cancer treatment. Some herbal gels have shown enhanced penetration, further supporting their use[19]. Therefore, this study aims to develop a Ginseng Extract-enriched topical gel for the treatment of skin cancer.

II. MATERIALS

Carbopol-940 was sourced from Swapnroop Chemicals, Aurangabad. The materials and reagents used in this study included Glycerine, Span 80, Liquid Paraffin, Tween 80, Methyl Paraben, Propyl Paraben, and Triethanolamine, all of which were obtained from Loba Chemical, Mumbai. Ethanol was purchased from Molychem, Mumbai. All chemicals and reagents used in this research were of analytical grade.

Methods

Preparation of Ginseng Extract

To extract Panax ginseng, start by thoroughly drying the roots and grinding them into a fine powder. Place the powdered ginseng in a Soxhlet apparatus and use ethanol as the solvent, allowing it to cycle through for 6-8 hours. Once extraction is complete, filter the mixture to remove solid particles. Concentrate the filtered solution using a rotary evaporator at a low temperature (40-50°C) to evaporate the solvent, producing a concentrated extract. Finally, dry the concentrated extract to obtain a stable powder.

Formulation of Ginseng Extract-Enriched Topical Gel

Carbopol-940 as the gelling agent and sodium carboxyl methyl cellulose as the thickening agent were dissolved in 50 ml of double-distilled water with continuous stirring. The preservative solution was prepared by dissolving the required amounts of preservatives in 5 ml of double-distilled water using a heated water bath. After cooling, glycerin was added to the preservative solution, which was then combined with the initial gel base. A measured quantity of Ginseng Extract was added and mixed thoroughly for homogeneity. Finally, the pH was adjusted to match skin pH (6.8–7) by adding triethanolamine drop by drop with continuous stirring until the gel reached the desired viscosity and consistency (Table 1).

Table 1. Formulation table of Ginseng Extract-Enriched Topical Gel

Ingredients	Quantity				
	F1	F2	F3	F4	F5
Ginseng Extract (mg)	500	500	500	500	500
Carbopol-940 (g)	1	1	2	1	3
Sodium CMC (g)	1	2	1	3	1
Glycerin (ml) (g)	2	2	2	2	2

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Methylparaben (0.5%) (ml)	0.3	0.3	0.3	0.3	0.3
Propylparaben (0.2%) (ml)	5	5	5	5	5
Triethanolamine (ml)	q. s.	q. s.	q. s.	q. s.	q. s.
Purified water (ml)	100	100	100	100	100

II. EVALUATION OF GINSENG EXTRACT-ENRICHED TOPICAL GEL

Physical appearance

Physical parameter such as color and appearance were checked visually.

Measurement of pH

The pH of the gel formulations was measured using a digital pH meter, calibrated with standard buffers at pH 4.0 and 9.0, by inserting the electrode directly into the gel[20].

Spreadability

Spreadability was assessed by placing 0.5 g of gel within a pre-marked 1 cm diameter circle on a glass plate. A second glass plate was placed over the gel, and a 50 g weight was applied on the upper plate for 5 minutes. The increase in the circle's diameter, measured in centimetres, was recorded as a comparative value for spreadability[21].

$$S = M * L/T$$

where S is the spreadability, M is the weight in pan, L isthe length moved by the glass slide, and T is the timetaken to separate the slide completely from each other.

Extrudability

The formulation was filled into a clean, collapsible aluminum tube and placed in a hardness tester. The plunger was adjusted to securely hold the tube, and pressure was applied for 30 seconds. The percentage of gel extruded was then calculated[22].

Viscosity

The viscosity of the gel formulations was measured at 37°C using a Brookfield DV-E viscometer. Spindles 3 and 4 were immersed in a beaker containing the gel, and the viscosity was recorded[23].

Homogeneity

Homogeneity of gel was tested through visual inspection for presence of any aggregates. It also can be tested by applying on the skin of a hand[24].

Stability studies

Accelerated stability studies were conducted on the optimized F3 formulation at 40 ± 2°C and 75 ± 5% relative humidity over a period of 3 months. The gel was stored in aluminum tubes, and its physicochemical properties, physical appearance, and viscosity were periodically evaluated using the same methods applied in the initial gel assessments[21].

III. RESULT AND DISCUSSION

Evaluation of Ginseng Extract-Enriched Topical Gel

Ginseng Extract gel formulations were prepared using varying concentrations of Carbopol-940 as the gelling agent and sodium CMC polymer, while keeping the concentrations of all other excipients, including Ginseng Extract, constant. This was done to assess the impact of the gelling agent and polymer concentrations. The resulting herbal gels were physically examined and found to be smooth with a faint brownish-yellow color. **pH measurement**

The pH of the Ginseng Extract gel formulations was measured using a digital pH meter. The pH of all the herbal gel formulations ranged from 6.62 to 6.94. The pH values of the formulations are presented in Table 2 and Figure 1.

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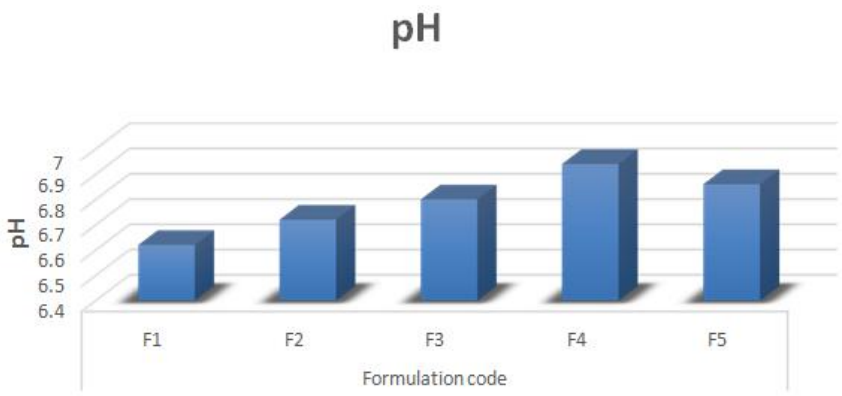

Figure 1: pH of Ginseng Extract gel formulations

Spreadability

All the prepared Ginseng Extract gel formulations were evaluated for spreadability. The spreadability of the herbal gels ranged from 15.70 to 24.37 gm.cm/s. An increase in the concentration of sodium CMC resulted in improved spreadability of the formulations. The spreadability values for all formulations are presented in Table 2 and Figure 2.

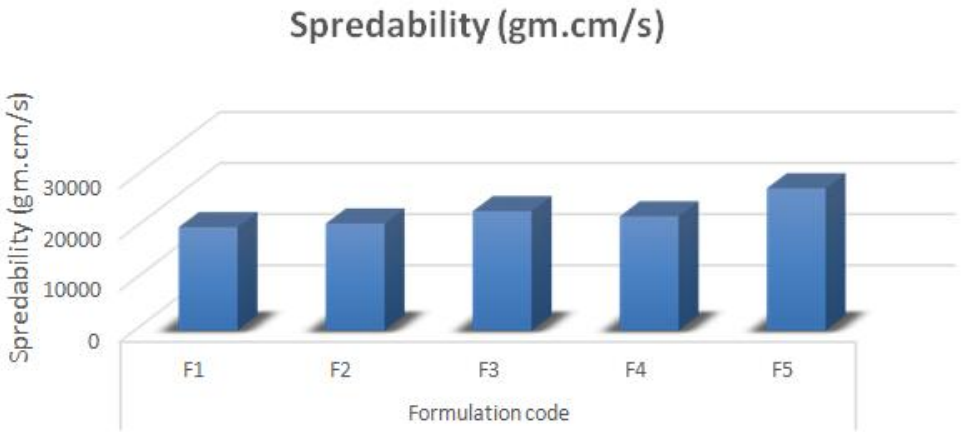

Figure 2: Spreadability of Ginseng Extract gel formulations

Extrudability

All the prepared Ginseng Extract gel formulations were evaluated for extrudability. The extrudability ranged from 85.51% to 90.45% w/w, indicating good extrudability. The extrudability values for all formulations are presented in Table 2 and Figure 3.

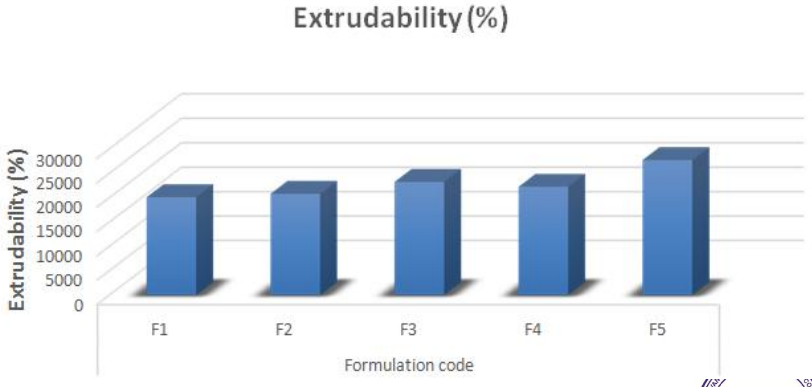

Figure 3: Extrudabilityof Ginseng Extract gel formulations

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Viscosity

The viscosity of the Ginseng Extract gel formulations was primarily influenced by the polymer content. As the ratio of polymer increased, the viscosity of the formulation also increased. The viscosity values for all formulations are provided in Table 2 and Figure 4.

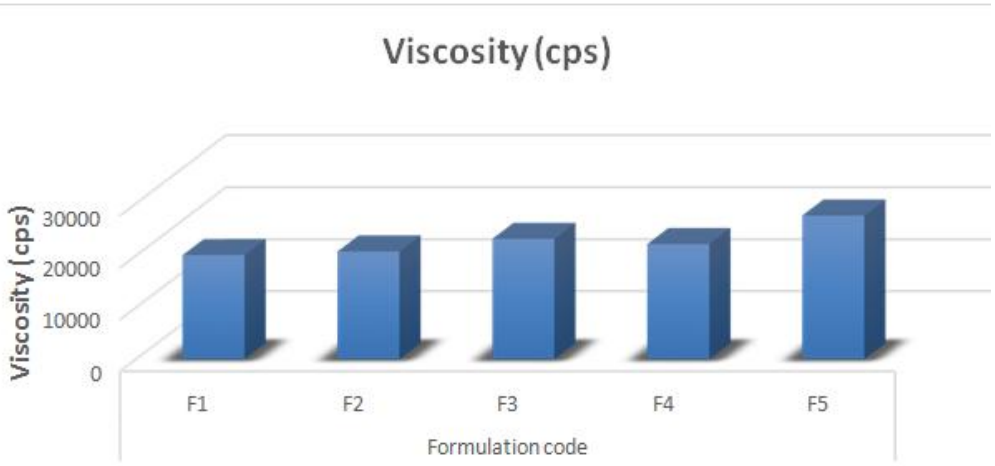

Figure 4: Viscosity of Ginseng Extract gel formulations

Homogeneity

All batches of the Ginseng Extract gel formulations demonstrated good homogeneity, with no lumps present. Most of the formulations showed excellent uniformity, with no grittiness observed

Table 2. Evaluation parameters of Ginseng Extract gel formulation

Parameter	Formulation code				
	F1	F2	F3	F4	F5
pH	6.62	6.72	6.80	6.94	6.86
Spreadability (gm.cm/s)	15.70	20.98	16.80	24.37	17.21
Extrudability (%)	87.63	85.51	90.45	89.63	87.25
Viscosity (cps)	20100	20800	23230	22230	27700

Stability studies

After storing the F3 formulation for 3 months at 40 ± 2°C and 75 ± 5% RH the gel was checked for physicochemical screening. The colour of the gel was brownish-yellow, homogenous, smooth texture and no crystallization of any kind was observed. The pH of F3 formulation was observed to be 6.85, viscosity was 23270 cps. Thus, all the phytochemical characteristics of the gel was similar to the initial time (0 month) giving evidence for its stability.

III. CONCLUSION

In conclusion, the Ginseng Extract-Enriched Topical Gel demonstrated promising potential as a therapeutic formulation for the prevention of epidermoid carcinoma. The gel's design, utilizing Carbopol-940 as the gelling agent and sodium CMC polymer, resulted in a stable, homogenous, and effective formulation. The characterization studies confirmed that the gel exhibited desirable properties, including appropriate pH, spreadability, extrudability, and viscosity, essential for topical application. Moreover, the incorporation of Ginseng Extract enhanced the gel's bioactive potential, making it a viable candidate for combating skin cancer. The formulation's ability to target cancer cells through a topical route, while minimizing systemic side effects associated with conventional therapies, positions it as a promising, patient-friendly alternative in the management of epidermoid carcinoma. Further clinical studies and trials are warranted to fully assess its efficacy and therapeutic potential in treating skin cancer.

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