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Efficacy of garlic emulgel using various gelling agents

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ABSTRACT

The aim of the present research work was to investigate the potential of emulgel in enhancing the topical delivery of Garlic. Emulgel formulations of Garlic were prepared using various gelling agents like Carbopol 934, gelatin and sodium alginate. The influence of the type of the gelling agent and the concentration of both the oil phase and emulsifying agent on the drug release from the prepared emulgel was investigated. The main purpose of this research was to design formulate and evaluate a topical gellified emulsions (Emulgel) of Garlic by different gelling agents. This Carbapol possesses very high viscosity, transparency, film forming properties at low concentration and reported to be useful in formation of gel with an objective to increase transparency and spreadability. All the prepared emulgel (F1,F2,F3) showed acceptable physical properties concerning color, homogeneity, consistency, spreadability, and pH value. The influence of the type of gelling agent on the drug release from the prepared emulgels was investigated and carbopol 934 (F3) showed good results not only in the drug release but also in physical evaluation parameters. From the drug release studies, the prepared formulation showed 90% of drug release in 6 h with good clarity and physical appearance and viscosity cps. Stability studies showed that the physical appearance, rheological study, zone of inhibition, and anti-microbial activity in the prepared emulgel remained unchanged upon storage for 3 months. It was finally concluded that the prepared formulation with Carbopol 934 (F3) was found to be more promising formulations as it shows better physicochemical characteristics and Antimicrobial activity.

Keywords: Garlic, Emulgel, Topical gel, Anti-microbial, Carbopol 934,gelatin, sodium alginate

INTRODUCTION

An emulsion is a biphasic liquid dosage form. An emulsion is a mixture of two or more liquids that are normally immiscible to each other but using emulsifying agents one liquid is dispersed into other liquid as droplets. So, there are two phases in an emulsion. One is the dispersed phase and another is the continuous phase. The concept is a dispersed phase (liquid), which is dispersed or spread in the other phase (continuous phase).

Types of Emulsion

Simple Emulsion

- Oil in Water (O/W) Emulsion
- Water in Oil (W/O)Emulsion

Multiple Emulsions

- Water-in-Oil-in-Water (W/O/W) Emulsion
- Oil-in-Water-in-Oil (O/W/O) Emulsion

Micro Emulsions

Size of droplets 10- 200nm

- Oil-in-Water Micro Emulsions
- Water-in-Oil Micro Emulsions

Uses of Emulsion

Emulsions are used for the administration of nutrients, drugs, and diagnostic agents. Topical creams and lotions are popular forms of emulsions for external use.

Emulsifying agents

Natural emulsifying agents

- **Vegetable sources-** Agar, Tragacanth, Gum acacia, etc.
- **Animal sources-** Wool fat, Gelatin, etc.

Semi-synthetic emulsifying agents

- Methylcellulose, Sodium CMC, etc

Synthetic emulsifying agents

- **Anionic emulsifying agents:** Sodium lauryl sulfate(SLS)
- **Cationic emulsifying agents:** Benzalkonium Chloride
- **Non-ionic emulsifying agents:** Glyceryl ester
- **Inorganic emulsifying agents:** Milk of magnesia

Gelling agents are the gel-forming agents when dissolved in a liquid phase as a colloidal mixture forms a weakly cohesive internal structure. They are organic hydrocolloids or hydrophilic inorganic substances. In semisolid dosage form, gelling agents are used at a concentration of 0.5%–10%.

Uses of gelling agents

Gelling agents are used to provide a three-dimensional structural network having a high degree of physical/chemical cross-linking to produce semisolid systems when dissolved or dispersed in an appropriate media.

Examples

Tragacanth, pectin, starch, carbomer, sodium alginate, gelatin, cellulose derivatives, polyvinyl alcohol clays, etc.
Emulgel has emerged as a promising drug delivery system for the delivery of hydrophobic drug. When gel and emulsion are used in combined form they are referred as Emulgel. In fact, the presence of a gelling agent in the water phase converts a classical emulsion into an emulgel. Both oil-in-water and water-in-oil emulsions are used as vehicles to deliver various drugs to the skin. Emulsions possess a certain degree of elegance and are easily washed off whenever desired. They also have a high ability to penetrate the skin.
Emulgel for dermatological use have several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non staining, water-soluble, longer shelf life, bio-friendly, transparent and pleasing appearance. The present work high lights the importance of Garlic shows a wide range of antimicrobial activity.
Alliin is present in the garlic, when Garlic cloves are crushed then enzyme Allinase is converted alliin into the allicine and allicine is again forms many sulphide compounds.
Garlic consist of sulfur containing compounds such as allicin, alliin, ajoene, diallyl disulfide, dithiin and Sallylcysteine. These large number of sulfur compounds are gives the smell and taste to the garlic. Diallyl disulfide is an important component in the garlic and being a powerful antibiotic and antifungal compound, Garlic is very largely used in spice due to its specific odor and taste and it is also reduces blood pressure and Heart problems.
From the research it was found that diallyl disulphide is a drug with broad-spectrum anti-cancer effects. It can inhibit the growth of various tumor cells, such as human colon cancer cells human gastric and breast cancer cells.
Diffusion is a mechanism of drug transport for the emulgel formulation.

Step.1 Percutaneous Absorption that gives concentration gradient
Step.2 Driving force for the drug movement across the skin
Step.3 Release of the drug from the vehicle
Step.4 Drug diffusion across the layers of the skin

MATERIALS AND METHODS

Materials

Garlic fine powder were purchased on online Amazon, Ethanolic extract of Garlic powder and distilled water were prepared in laboratory of department of pharmaceutics., Oleic acid, Propylene glycol, Methyl salicylate, Cetostearyl alcohol, Tween 20, Carbopol 934, Distilled water, Propyl, Triethanolamine are of analytical grade.

Equipment used

Electrical balance (Citizen), Hot air oven (BIO Tecnics India), PH-meter (Equiptronics Model NO. EQ-602), Sonicator (Citizen), Magnetic stirrer (Remi Electrotecnik LTD), UV spectrophotometer-1800 (Shimadzo Japan).

Methods

Preparation method of Garlic Emulgel

Gel preparation

The gelling agent was prepared by dispersing required quantity given in formulation table and in the given quantity of purified water with constant stirring at a moderate speed and soaked overnight.

Emulsion preparation

The oil phase of emulsion was prepared by mixing oleic acid, methyl salicylate, tween 20 and previously melted cetostearyl alcohol. Methyl paraben, propyl paraben were mixed in propylene glycol this added this mixture was dissolved in aqueous phase. Then oil phase was mixed slowly with aqueous phase with constant temperature (50-600C).

Emulgel preparation

The obtained emulsion was mixed with the gel subjected to homogenization for 2 hours to get Garlic Emulgel. The pH was adjusted to 6-7 using triethanolamine.

Table 1: Formulation of Garlic emulgel

Ingredients	FORMULATION F1	FORMULATION F2	FORMULATION F3
Garlic %	0.4	0.4	0.4
Oleic acid (%)	20	20	20
Oleic acid (%)	20	20	20
Methyl salicylate (%)	10	10	10
Propylene glycol (%)	5	5	5
Methyl salicylate (%)	10	10	10
Cetostearyl alcohol (%)	4	4	4
Tween 20 (%)	3.2	3.2	3.2
Carbopol 934 (%)	-	-	1.6
Gelatin	-	1.6	-
Sodium alginate	1.6	-	-
Distilled water (q.s) (%)	100	100	100
Propyl paraben (%)	0.02	0.02	0.02
Methyl paraben (%)	0.02	0.02	0.02
Triethanolamine	Adjust pH 6-7	Adjust pH 6-7	Adjust pH 6-7

Characterization of Emulgel

Physical appearance

Formulations were evaluated for color, homogeneity and consistency. The physical appearance of all the formulations was noted.

pH Determination

pH evaluation of the topical formulation is more important as it may cause irritation to the skin if varied from normal skin pH conditions. Its determined using digital pH meter .The pH meter is dipped into the emulgel and the pH is checked.

Washability Test

Formulations were applied on the skin and then ease and extent of washing with water were manually checked.

Spreadability

Spreadability was checked by slip and drag character of the emulgel. To determine spreadability, the apparatus consisting of a wooden block is provided by a pulley at one end. In the block glass is fixed. 2g of emulgel is placed on it and is covered with another glass slide as a sandwich.one kg of weight is placed on it and the spreadability is checked.

Swelling Index

To determine the swelling index of prepared topical emulgel 1 gm. of gel is taken on porous aluminum foil and then placed separately in a petri plate containing 10 ml 0.1N NaOH. Then samples were removed from petri plate at different time intervals and put it on dry place for some time after it reweighed. Swelling index is calculated as follows:

$$\text{Swelling Index (SW)\%} = [(Wt. - Wo) / Wo] \times 100.$$

Where,

(SW) % = Equilibrium percent swelling,
Wo = Original weight of emulgel at zero time,
Wt. = Weight of swollen emulgel after time t.

Extrudability

It is a usual empirical test to measure the force required to extrude the material from tube. The method applied for determination of applied shear in the region of the rheogram corresponding to a shear rate exceeding the yield value and exhibiting consequent plug flow. In the present study, the method adopted for evaluating emulgel formulation for extrudability is based upon the quantity in percentage of emulgel and emulgel extruded from lacquered aluminum collapsible tube on application of weight in grams required to extrude at least 0.5 cm ribbon of emulgel in 10 seconds. More quantity extruded better is extrudability. The measurement of extrudability of each formulation is in triplicate and the average values are presented. The extrudability is than calculated by using the following formula:

Extrudability = Applied weight to extrude emulgel from tube (in gm.)/Area (in cm 2).

Rheological Study (Viscosity)

The viscosity of gel during handling, transport and storage is an important criterion. The viscosity of different Emulgel formulations was determined by using Brook field viscometer. The formulation whose viscosity was to be determined was added to the beaker and was allowed to settle down for 30 min at 25°C before the measurement was taken.Spindle was lowered perpendicularly into the center of the emulgel taking care that spindle does not touch the bottom of the jar and rotated at a speed of 50rpm for 10 min. The viscosity reading was noted.

Skin irritation study

As the preparation is an topical application the irritation test is very important. This test was carried out on the animal skin. The emulgel is apllied to the animal skin, and then the animals are returned to the cages. After 24 hrs the animals are tested. Then the emulgel are removed from the site and noted.

Stability studies

The prepared emulgels were packed in aluminium collapsible tubes (5g) and subjected to stability studies at 5 c,25 c /60%RH,30 c/65%RH,and 40 c/75%RH for a period of 3 months. Samples were withdrawn at 15 day intervals and evaluated.

Determination of zone of inhibition

Anti-microbial activity was checked by agar diffusion method. The culture were grown in nutrient broth and incubated at 37°C, for 24 hrs. After incubation periods was over, 0.1 ml of culture was seeded in 25 ml molten nutrient agar butts, mixed and poured into sterile petri plates and allowed to solidify. The well was bored with 6 mm borer in seeded agar. 0.1 g of each ointment sample was added in each well. Plates were kept at 10°C as a period of pre diffusion for 30 minutes. After it normalized to room temperature; the plates were incubated at 37°C for 24 hrs in case of bacteria and at 27°C for 48 hrs in case of fungi. After incubation period was over, the zone of inhibition was measured with help of Hi-antibiotic zone reader.

Dilution test

50 to 100 times aqueous dilution of emulgel was done by adding Continuous phase and visually checked for phase separation.

RESULT

Characterization of Emulgel

Physical appearance

Table 2: Physical appearance data

S.No	Parameters	F1	F2	F3
1.	Color	Yellow	Yellow	Yellow
2.	Homogeneity	Homogeneous	Homogeneous	Homogeneous
3.	Consistency	Slightly stiff	Stiff	Semisolid

PH determination

Table 3: pH of Emulgel

S.No	Formulation	pH value
1	F1	7.2
2	F2	6.9
3	F3	7.0

Washability

Table 4: Washability of Emulgel

S.No	Formulation	Washability
1	F1	Better
2	F2	Not bad
3	F3	Good

Spreadability

Table 5: Spreadability of Emulgel

S.No	Formulation	Spreadability Length(cm)
1	F1	5.9

2	F2	6.1
3	F3	6.3

Swelling Index

Table 6: Swelling Index of Emulgel

S.No	Formulation	Swelling Index %
1	F1	24.02
2	F2	27.34
3	F3	29.05

Extrudability of Emulgel

Table 7: Extrudability of Emulgel

S.No	Formulation	Extrudability
1	F1	15.8
2	F2	16.4
3	F3	19.3

Viscosity of Emulgel

Table 8: Viscosity of Emulgel

S.No	Formulation	Viscosity (cp)
1	F1	1880
2	F2	1936
3	F3	2233

Skin irritation study

No allergic symptoms like inflammation, redness, irritation was observed on rats after 24hrs.

Stability study

F3 formulation was found to be stable after 3 months of storage. No change was observed in their characters.

Zone of inhibition

Table 9: Zone of inhibition

S.No	Formulation	Zone of inhibition(mm)
1	F1	19.32
2	F2	24.67
3	F3	29.54

Dilution Test

Table 10: Dilution Test

S.No	Formulation	Dilution Test
1	F1	No phase separation
2	F2	No phase separation
3	F3	No phase separation

DISCUSSION

Physical appearance

The prepared Garlic emulgel formulations were yellow colored preparation with a smooth and homogeneous appearance.

pH of the formulation

The pH values of all prepared formulation ranged from 6.9 to 7.0, which are considered acceptable to avoid the risk of irritation upon application to the skin because adult skin pH is average 5-7.

Washability

All the prepared formulations are easily washable and non-greasy

Spreadability

The values of spreadability indicate that the emulgel is easily spreadable by small amount of shear. Spreadability of Formulation F3 was good, indicating spreadability of emulgel containing carbopol 934 was good.

Swelling index

The swelling index of the optimized formulation F3 of emulgel was found to be excellent than other formulations.

Extrudability study (Tube test)

During the test, F3 formulation of 19.3 cm^2 weight required to extrude 1 cm ribbon of emulgel in 10 sec from aluminum collapsible tube, From the result consider that more quantity of emulsion based gel extrude at little applied pressure on tube which shows better emulgel have a good extrudability.

Viscosity

The measurement of viscosity of the prepared emulgel was done with Brookfield viscometer (Brookfield DV-E viscometer). The highest viscosity was found in F3 Formulation.

Skin irritation test

No allergic reactions was observed

Stability studies

Stability studies of optimized formulation F3 were performed. It can be observed that the emulgel formulation showed no major alteration in relation to the pH, consistency. The formulation F3 shows stability for the period of 3months. No significant changes in the pH, physical appearance and rheological properties of formulations was observed.

Optimization of formulation

The present work deals with the design and evaluation of Garlic topical Emulgel using gelling agent like carbapol 934 in different concentrations and all the raw materials are of standard grade as supplied by the manufacturer. The spreadability of emulgel formulation F3was good. The highest viscosity was found in F3 Emulgel formulation it may be due to carbopol gelling agent. Topical gel formulation was prepared by using carbapol 934 in different concentrations. The prepared formulations are yellowish in appearance. Optimized formulation F3 shows yellowish in appearance. pH was found with in the limit. Viscosity is important parameter for characterizing the gels as it affect spreadability, extrudability and release of the drug, The formulation should increase viscosity as the concentration of gelling agent increased optimized formulation F3 show ideal viscosity. Optimized formulation F3 shows better extrudability. Emulgel will act as depot of drug which releases drug in sustained manner. Hence the optimized formulation may be used to treat the topical Microbial diseases.

CONCLUSTION

Concluded that the prepared formulation with Carbopol 934 (F3) was found to be more promising formulations as it shows better physicochemical characteristics and Antimicrobial activity.

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CONFLICT OF INTEREST

There are no conflict of interest.

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