DEVELOPMENT OF TOPICAL FORMULATIONS CONTAINING BIOACTIVE VOLATILE OILS: RELATIVE CHARACTERIZATION OF DRUG RELEASE FOR CREAM OINTMENT AND GEL

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Abstracts

Topical or dermatological preparations are preferred for many of the dermatological conditions due to well-known undesired effects of oral drugs for skin care function. In recent times, some herbal drugs have also proved to have efficient skin care properties, which may also be used in clinical practice in the area of skin care. Such products are biocompatible and non-toxic. In this study garlic and ginger oil were used as a bioactive extract for development of topical formulation. Creams, ointment and gels were formulated and drug release form these formulation were studied. It has been found that gels were extremely suitable as a final formulation for bioactive oils.

Keywords: Allium sativum, Zingiber officinale Creams, Ointment, Gels.

Introduction

There are several reports in the ethno pharmacological literature regarding the antimicrobial activity of plant extracts¹. However, which plant part is responsible for activity, further which of the plant extractives are active, particularly on which organism, whether effective in skin pathogens is of much interest². They are most frequently caused by Staphylococcus aureus, Streptococcus mutans, and coryneform bacteria. Impetigo, folliculitis, boils, and erythrasma are common examples³. Systemic infections may also have skin manifestations. Secondary infections originate in diseased skin as a superimposed condition⁴. Intertrigo and toe web infections are examples of
secondary infections. One of the special needs of these formulations is that, they must be able to cling to the applied surface for a protracted period generally until being washed off or worn off. These formulations must be stable; compatible should have patients or consumer acceptability and promote efficient bioavailability of active ingredients. Ointments are greasy, semisolid preparation which are often anhydrous and which contain medicaments either dissolved or dispersed in the vehicle. Ointment bases are classified into hydrocarbons, fat and fixed oils, silicones, absorption bases, emulsifying bases and water soluble bases. The cream used in topical, denotes an emulsion with semisolid consistency, Formulated for application to skin or mucous membranes. Emulsions are heterogeneous system, consisting of either water droplets dispersed in oil or vice versa, stabilized by an emulsifying agent. Even complex o/w/o or w/o/w emulsion can be formulated. A cream of o/w type is useful as water washable bases or w/o type providing emolliency and cleansing action. Gels are the transparent to opaque semisolid dosage form containing high ratio of solvent to the gelling agent. Gelling agents when dispersed in appropriate solvent merge or entangled to form a three dimensional colloidal network structure. This network limits fluid flow by entrapment and immobilization of the solvent molecules. The network structure is also responsible for a gel’s resistance to deformation and therefore, its viscoelastic properties. Gel network formed exists as random coil, helix, stacks, and house of cards. Recently Allium sativum and Zingiber officinale was found to contain antimicrobial activity. From the ancient times these plants were used as for antimicrobial therapies. The new era of medicine prerequisites the formulation containing these oils for better therapeutic activity and treatment.

**Materials and Method**

Crud Allium sativum and Zingiber officinale, Carbopol-934, HPMC, CMC, HPC, Pluronic 127, Triethanolamine, Methyl Paraben 0.02g, Propyl paraben 0.02g, Propylene glycol/ PEG 400, Tween 20, Span 20. All reagents used were of analytical grade.
Volatile oil Extraction

As the plants selected were essential oil containing drugs the essential oil was extracted from these plants\textsuperscript{15}. The fresh plant parts after removing the protective covering and macerating for 12 hours were subjected to hydrodistillation for extraction of volatile oils. The extraction of volatile oil was carried out in Clavenger’s apparatus\textsuperscript{16}. The weighed drug was placed in the distillation flask with a mixture of water and glycerine and connected to receiver which is filled with water and connected to a condenser. On distillation, the oil and water condensed and essential oil which was collected in the graduated receiver as a layer on top of water was measured. The distilled volatile oils were dehydrated using anhydrous sodium sulphate and used for further studies. Glycerine (40\%) was added to fresh material to enhance penetration of water\textsuperscript{17}.

Preparation ointment, creams and gels:

Topical formulations oils as an ointment were formulated formulations and diffusion of extracts from these formulations was studied. Ointments were prepared by conventional method using the standard formulas in official books. Fusion method was used to prepare paraffin ointment I.P and cold cream\textsuperscript{18}. Gel was prepared by dissolving Carbopol 934 (1.5\%w/w) in purified water. It was soaked overnight in distilled water and then stirred with high speed stirrer. Drug oils were added and then again stirred. Triethanolamine was then added to it to adjust the pH. Carbopol 1-3\% were tried. Carbopol >2\% is highly viscous and have difficulty in application. Therefore Carbopol 1-2\% is selected for the formulations. The formula for preparation of ointment, cream and gels is shown in table-1.

Table: 1-Formula for ointment, creams and gels for \textit{Allium Sativum} and \textit{Zingiber officinale}

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Ointment</th>
<th>Cream</th>
<th>Gel</th>
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<tr>
<td></td>
<td>F-1/ P-1</td>
<td>F-2/ P-2</td>
<td>F-3/ P-3</td>
</tr>
<tr>
<td>Carbopol (% W/W)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HPC (% W/W)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Triethanolamine</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Methyl Paraben(g)</td>
<td>0.02</td>
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<td>0.02</td>
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<tr>
<td>Propyl paraben(g)</td>
<td>0.02</td>
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**In-vitro drug Release:**

In-vitro drug release studies were carried out using Franz diffusion apparatus fitted with excised rat abdominal skin\(^{19}\). The hairless skin of euthanized rat was first cleaned to remove any subcutaneous fat and was soaked in diffusion medium for one hour to saturate it before mounting it on diffusion cell. The skin was mounted on Franz Diffusion Cell with epidermis facing the donor compartment. The extract / formulation were applied to stratum corneum surface. The cell had an effective receptor solution volume of 12 ml and a skin surface area of 3.14 cm\(^2\). The receptor compartment was filled with pH 6.4 phosphate buffer saline (PBS) and it was stirred at 600 rpm using small magnetic bar for uniform mixing of the contents, the temperature was maintained at 37°c ± 1°c. 1ml of sample was withdrawn from the receptor compartment after each 1 hour interval and the same was replenished using fresh buffer solution to maintain the sink conditions. Samples 10% were diluted with 40% surfactant solution (Tween 80 HLB 15& Acconon CC-6 HLB 6 in 1:1 ratio) and 50% 6.4 PBS. Samples were analyzed spectrophotometrically. The method reported by Gholap and Bandopadhyay for spectrophotometric determination of essential oil of *Curcuma amada* was used for determination of \(\lambda_{\text{max}}\) (peak absorbance) of various extracts and essential oils\(^{20}\). In the beginning of the release studies, for the estimation of essential oils from the formulations, standard calibration curves were prepared by UV spectrophotometric methods\(^{21}\). Standard stock solutions were prepared by dissolving the volatile oils in ethanol and the extracts in methanol. These stock solutions were suitably diluted using ethanol/methanol and pH 6.4 saline phosphate buffer to obtain working standard solutions in range of 2-40µg/ml and the absorbance of these solutions was read on a double beam UV spectrophotometer (UV-1700 PharmaSpec UV visible spectrophotometer, SHIMADZU, Kyoto, Japan) at 366nm and 276nm respectively. Saline Phosphate buffer pH 6.4 was prepared by dissolving 1.79 g of disodium hydrogen phosphate, 1.36g of Potassium dihydrogen phosphate and 7.02g of sodium Chloride in distilled water upto1000ml.

<table>
<thead>
<tr>
<th></th>
<th>PEG 400 (%W/W)</th>
<th>Tween 20 (%W/W)</th>
<th>Span 20 (%W/W)</th>
<th>5</th>
<th>10</th>
<th>15</th>
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<th>0.6</th>
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<tr>
<td></td>
<td>0.2</td>
<td>0.6</td>
<td>0.8</td>
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</table>
Results and Discussion

Formulation of *Allium Sativum* and *Zingiber officinale* were studied for drug release. All the volatile oils showed a good percutaneous absorption through hairless rat skin. The % release of volatile oil of *Allium Sativum* and *Zingiber officinale* through micro porous membrane was significantly higher in Carbopol gel as compared to ointment and creams. Variation in drug release was observed with volatile oil of *Allium Sativum* and *Zingiber officinale*. Ointments and creams show initial burst release of drug with incomplete release at the end of diffusion study. Ointments also show unbalanced release with time. The cumulative release study reveals that there is incomplete discharge of drug from creams over the 8 hours of diffusion.

**Fig: 1 Cumulative drug release from ointment (Allium Sativum)**

![Fig 1 Cumulative drug release from ointment (Allium Sativum)](image)

**Fig: 2 Cumulative drug releases from Creams (Allium sativum).**

![Fig 2 Cumulative drug releases from Creams (Allium sativum)](image)
Fig: 3 Cumulative drug releases from Gels (Allium sativum).

Fig: 4 Cumulative drug releases from Ointment (*Zingiber officinale*).

Fig: 5 Cumulative drug releases from Cream (*Zingiber officinale*).
Fig: 6 Cumulative drug releases from Gels (*Zingiber officinale*).

Fig: 7 Cumulative drug releases (*Allium Sativum*).

Fig: 8 Cumulative drug releases (*Zingiber officinale*)
In both *Allium Sativum* and *Zingiber officinale* volatile oil formulation, gel shows excellent release characteristics. Though creams and ointment are widely used for the antimicrobial preparation, gels can serve as a good option for herbal drugs. In this study, drug release characteristics clearly indicate the ability of gels to withstand large amounts of drug over the period of time. Creams and ointment were found to be unpredictable for the release from *Allium Sativum* and *Zingiber officinale*. The drug release characteristics of ointment, cream, and gels were shown in figures 1-8. Figures clearly indicate the usefulness of gel over creams and ointment for bioactive oils extracted from herbals. Ointments become easily rancid as they contain oleaginous bases and are not stable at high temperatures. Creams being thermodynamically unstable systems are not stable at very low or high temperatures and break easily. Moreover, they produce difficulties in sterilization. Gels are smooth dispersions of synthetic macromolecules, so do not promote growth of micro-organisms, can be sterilized easily and are stable at low as well as high temperatures.

**Conclusion:**

A Clear finding from this study is that gels were superior to creams and ointment for herbal formulation. Volatile oil release from gels was progressive with time and can be useful for sustained delivery of antimicrobial bioactive extracts. Further, gels were found to show almost complete release of medicament derived from herbal origin.

**References**


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