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Research Article

NOVEL FORMULATION FOR ENHANCED EFFICACY OF *LAVANG TAILA* (CLOVE OIL) FOR ANTI-INFLAMMATORY ACTIVITY

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ABSTRACT

Lavang (Clove - *Eugenia caryophyllata*) has been used since years for its analgesic, anti-inflammatory and anesthetic effects. The aim of current study was to observe anti-inflammatory activity of clove oil in the form of 'Bio-adhesive Gel', since it has property to inhibit COX-2 enzyme and prostaglandins.

'Self-Micro emulsifying Drug Delivery System (SMEDDS)' is an isotropic and thermodynamically stable mixture of oil, surfactant/co-surfactant and drug. A novel SMEDDS of extract of Clove (*Lavanga Taila*) and other chemicals as 'Vitamin E TPGS' - as surfactant, antioxidant, penetration enhancer and can protect the oil from degradation, 'Transcutol P'- as co-surfactant, 'Ethanol'- co-solvent,' Carbopol' - as the gelling agent and Distilled water. Carrageenan induced rat paw edema model was used to investigate the *in vivo* performance. Commercial clove oil formulation was used as reference formulation.

After the carrageenan injection, the paw volumes were measured at 15 min, 30 min, 1 hour, 2 hours, 3 hours by using a plethysmometer. The percentage inhibition of edema was calculated by the equation: % inhibition of edema = 100 [1-(Vt/Vc)].

Various proportions of the contents were used to prepare several 'SMEDDS' formulations. The optimized batch was selected on the basis of clarity and stability for 24 hrs. Organoleptic parameters such as pH value (7.3), Spreadability (++), Consistency(+++), Washability (+++), Irritation(None), Film formation (continuous) were observed for the prepared gel.

Results reveal that the action of 'SMEDDS gel' was about two times better than the clove oil alone, as the percentage of inhibition of edema was 42.06 % by 'SMEDDS gel' while the Clove oil inhibits 25.67% at the end of 3rd hour. The *in vivo* studies showed that bio-adhesive gel of clove oil has significant role as anti-inflammatory (*Shothahar*) action. The gel can be further used for oral preparations. However more investigations are needed to elucidate the exact mechanism of the gel.

KEYWORDS: *Lavang taila* (Clove oil), SMEDDS, Anti-inflammatory activity, Rat-paw edema test.

INTRODUCTION

Since long skin is a widely used as a potential route of delivery of local and systemic drugs in the form of micro/nano particles. The skin also provides a natural physical barrier against particle penetration, but there are opportunities to deliver therapeutic agents, especially in diseased skin and to the openings of hair follicles.[1] In Ayurveda *Snehana*, *Swedana*, *Lepana* are some of the modalities of treatment applied on the skin. [2] Whilst in modern health science it has been used for the topical delivery of compounds, since the 1970s with the advent of transdermal patches that it has widely been used as a route for systemic delivery. Nanoparticle/micro particle delivery through the skin is being increasingly used to facilitate local therapies.[3]

A topical medication is applied to the body surfaces such as the skin or mucous membranes to treat ailments with the help of a large range of classes including but not limited to creams, foams, gels, lotions and ointments. In order to enhance drug transdermal absorption, different methodologies have been investigated, developed, and patented. Improvement in physical permeation-enhancement technologies has led to renewed interest in transdermal drug delivery. Some of these novel advanced transdermal permeation-enhancement technologies include iontophoresis, electroporation, ultrasound, micro needles to open up the skin, and more recently the use of transdermal nanocarriers.[4]

Lavanga (Clove)

Lavanga is the dried flower bud of *Syzygium aromaticum* (Linn.) Merr. & L.M. Perry Syn. *Eugenia aromatica* Kuntze, *Eugenia caryophyllata* Thunb. (Fam. Myrtaceae), a tree cultivated in many parts of the. world and also to a considerable extent in South India: flower buds collected twice a year, In the months of October and February when they change colour from green to crimson, dried carefully and separated from their peduncles.

Synonyms of *Lavang*- Sanskrit: *Devapushpa*; Assamese: *Lavang*, *Lan, Long*; Bengali: *Lavang*; English: Clove; Gujrati: *Lavang*, Laving; Hindi: *Lavanga, Laung*; Kannada: *Lavanga*; Kashmiri: Rung; Malayalam: *Karampu*, *Karayarnpoovu*, *Grampu*; Marathi: *Lavang*; Oriya: *Labanga*; Punjabi: *Laung*, Long; Tamil: *Kirambu, Lavangam*; Telugu: *Lavangalu*; Urdu: *Qarnful, Laung.*

According to Ayurveda its Properties and actions are -

Rasa: *Katu, Tikta;* ***Guna:*** *Laghu, Tiksna;* ***Virya:*** *Sita;* ***Vipaka:*** *Katu;* ***Karma:*** *Sulahara, Dipana, Kasahara, Kaphapittasamaka, Pacana* and *Rucya.*

Therapeutic uses: *Shoth, Shoola, Amlapitta, Svasa, Chardi, Adhmana, Hikka, Kasa, Trsna*.[5]

Its Chemical properties are - Clove buds yield approximately 15% to 20% of a volatile oil that is responsible for the characteristic aroma and flavor. The bud contains a tannin complex, gum and resin, and a number of glucosides of sterols. The principal constituents of distilled clove bud oil (60% to 90%) are the phenylpropanoids, including primarily eugenol (4-allyl-2-methoxyphenol) and carvacrol, thymol, and cinnamaldehyde. Major components in the bud oil from India are eugenol (70 %) followed by β- caryophyllene (19.5%) and eugenyl acetate (2.1%) and small quantities of gallic acid, sesquiterpenes, furfural, vanillin, and methyl-n-amyl ketone. Other constituents include flavonoids, carbohydrates, lipids, oleanolic acid, rhamnetin, and vitamins. Similarly it containseugenol, caryophyllene, humulene, and eugenyl acetate.[6][7][8][9]

Self Micro-Emulsifying Drug Delivery Systems (SMEDDS)

SMEDDS is an isotropic and thermodynamically stable mixture of oil, surfactant/co-surfactant and drug.[10] SMEDDS are defined as isotropic mixtures of natural or synthetic oils, solid or liquid surfactants, or alternatively, one or more hydrophilic solvents and co-solvents/ surfactants have an unique ability of forming fine oil-in-water (o/w) micro-emulsions upon mild agitation.[11]

Literatures have shown that clove oil has anti-inflammatory property too[12]. It has also been used topically for drug delivery. But the major limitation of using oil is it is too concentrated and cannot remain in contact with skin for long time. So, there is a need of formulating such a formulation which will solve the as mentioned problems.

Current work has been done for formulating SMEDDS of Clove oil and evaluating its anti-inflammatory activity.

MATERIALS AND METHOD

1. Materials

Extract of Clove (*Lavanga Taila*) and other chemicals used were 'Vitamin E TPGS' (d-alpha Tocopheryl polyethylene glycol 1000 succinate)- is used as surfactant as well as it acts as antioxidant and can protect the oil from degradation, 'Transcutol P'- as co-surfactant, 'Ethanol'- co-solvent,' Carbopol' - as the gelling agent and Distilled water.

2. Method

(i) Preparation of SMEDDS concentrate

The 'Self Micro-Emulsifying Drug Delivery Systems (SMEDDS)' are easily prepared by simple admixing of ingredients. Here in the 'Clove oil' was first mixed with the 'Vit. E TPGS' and 'Transcutol P', then ethanol was added to it drop wise to form a clear solution.

(ii) Incorporation of SMEDDS in gel

'Carbopol 980' was taken as the gelling agent. The 'SMEDDS' concentrate was mixed with the gelling agent to form 1.5% w/v of carbopol gel. This is the finished product. The optimized batch was taken as final concentrate. Batches taken are given in table 1.

(iii) Rat paw-edema test

Anti-inflammatory activity was evaluated using carrageenan-induced rat paw edema method. Carrageenan (0.1 ml of 1% w/v suspension) was injected into the sub plantar region of the both the hind paw of each rat. The right hind paw was kept as control and left hind paw was considered as test one. After the carrageenan injection, the paw volumes were measured at 15 min, 30 min, 1 hour, 2 hours, 3 hours by using a plethysmometer. Edema was expressed as the mean increase in paw volume relative to control. The percentage inhibition of edema was calculated by the following equation:

% inhibition of edema = 100 [1-(Vt/Vc)]

Where, Vc = edema volume in the control

Vt = edema volume in test.

(iv) Organoleptic Parameters

Prepared gel was evaluated based on its appearance, texture and consistency. Texture was determined on the basis of grittiness/smoothness. Texture should be smooth so it can be spreadable and washable easily.

(v) pH value

10% w/v homogenous solution of gel was prepared and then pH was calculated by pH meter.

(vi) Effect on skin

- Spreadability

Spreadability was determined by applying the lotion slowly on the skin.

- Skin feeling (Oily/Greasy)-

  Skin feeling was noted as either Greasy or not.

- Film formation-

Film formation was determined on the basis of its uniformity (continuous/not).

- Washability

  Washability was checked by keeping applied skin area under the tap water for about 10 min.

RESULTS & DISCUSSION

As mentioned in table no. 1 several 'SMEDDS' formulations (T1, T2, T3, T4, T5) were prepared using various proportions of 'Clove oil', 'Vit. E TPGS', 'Transcutol P', 'Ethanol' and 'Carbopol 980'. The optimized batch was selected on the basis of clarity and stability for 24 hrs. 'Batch T5' was found to be stable in terms of clarity and no precipitate was found. On dilution oil globules did not

separate. Therefore, 'Batch T5' was considered as optimized.

Table 1. Trials of SMEDDS formulations

Ingredients	T1	T2	T3	T4	T5
Clove-oil (%w/w)	0.5	0.2	0.2	0.5	0.5
Surfactant (%w/w)	0.5	0.2	0.1	0.5	0.5
Co-surfactant (%w/w)	0.2	--	--	0.2	0.2
Co-solvent (%w/w)	0.5	0.2	0.1	0.2	0.3

The organoleptic properties viz. 'spreadability', 'consistency', 'washability', 'film formation' and 'irritation' were evaluated for the prepared gel (table 2) so that the gel should be spread in equal amount, it should be washed out easily and any adverse reaction should be avoided on the desired area where the gel was applied.

Table 2. Organoleptic test results of prepared gel

Test parameters	Observations
pH	7.3
Spreadability	++
Consistency	+++
Washability	+++
Irritation	Not observed
Film formation	Continuous

Table 3 shows comparative results of rat paw edema test of 'clove oil as such' v/s 'SMEDDS gel'. Results reveal that the action of 'SMEDDS gel' was about two times better than the clove oil alone, as the percentage of inhibition of edema was 42.06 % by 'SMEDDS gel' while the Clove oil inhibits 25.67% at the end of 3rd hour.

Table 3. Comparative rat paw edema test results

Formulation	% inhibition with time				
	15 min	30 min	1 hr	2 hr	3 hr
Clove oil	14.9	17	18.7	22.17	25.67
SMEDDS Gel	23.67	28.78	34.04	38.78	42.06

CONCLUSION

Lavanga Taila (Clove oil) could be applied as micro-formulations which can increase its efficacy and effect. The accompanying substances like 'Vit. E TPGS' as surfactant has natural source, it acts as anti-oxidant and makes the system more stable, 'Transcutol P' as co-surfactant facilitates functions of surfactant, it also helpful in reduction of particle size, and 'Ethanol' as co-solvent which prevents the precipitation of the product. Small amount of 'Carbopol 980' increases the soaking property of the gel as well as augments stability of the formulation for long period. The Organoleptic test results of prepared gel like spreading ability, consistency, washability, film formation are also noteworthy. The result proves that SMEDDS gel is significantly effective in inflammatory condition as the edema inhibits 42.06 % in the minimal time period.

Future scope

The gel prepared can be further used for dental preparations and for giving sustained action using some sustained release polymers.

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