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Development and Evaluation of Antiarthritic Herbal Ointment

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ABSTRACT

Formulation and evaluation of antiarthritic (anti-inflammatory) herbal preparation (Ointment) containing Menthol and Methyl Salicylate. The Ointment formulation was designed by using five different ointment bases. Various formulation batches containing 5% Menthol and 15% Methyl Salicylate were prepared. Clove Oil was used as a penetration enhancer. The optimized herbal ointment formulations was subjected to stability studies and evaluated for pH, Viscosity and Rheological studies, Spreadability, Washability. Final formulations along with market preparation were evaluated for its topical anti-inflammatory activity against carrageenan induced Rat-paw edema on wistar rats of either sex. Ten Ointment formulations were prepared successfully and evaluated for the physical properties, skin feeling, stability study and anti-inflammatory activity. Formulation containing 5% Menthol, 15 % Methyl salicylate and 1 % Clove oil and water miscible ointment base showed better % inhibition of edema compared to others. Ointments containing 1 % Clove oil showed better Anti-arthritic (Anti-inflammatory) activity in all five ointment base. From the present study we concluded that the water miscible base worked as the best carrier for the drug (5% Menthol and 15% Methyl Salicylate) in concern with stability as well as for the anti-inflammatory activity of the ointment. The optimized ointment formulation showed better inhibition of the inflammation as compared to conventional marketed formulation.

Keywords: Herbal Antiarthritic ointment, Menthol, Methyl Salicylate, Clove oil, Rat paws edema method

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INTRODUCTION

Ointments are used topically for several purposes, e.g., as protectant, antiseptics, emollients, antipruritic, kerotolytic, and astringents. The vehicle or base of an ointment is of prime importance if the finished product is expected to function as any one of the above categories. In the case of a protective ointment, it serves to protect the skin against moisture, air, sun rays and other external factors. It is necessary that the ointment neither penetrates the human skin barriers nor facilitates the absorption of substances through this barrier. An antiseptic ointment is used to destroy or inhibit the growth of bacteria. Frequently bacterial infections are deeply seated; a base which has the capacity to either penetrate or dissolve and release the medication effectively is therefore desired. Ointments used for their emollient effect should be easy to apply, be non-greasy and effectively penetrate the skin.

There are five types of ointment bases on the basis of their physical composition. Each has different physical characteristics and therapeutic effectiveness [1]. i.e.

- Oleaginous bases
- Absorption bases
- Water in oil emulsifying bases
- Oil in water emulsifying bases
- Water soluble or water miscible bases

It is the ability of Menthol to chemically trigger the cold-sensitive TRPM8 receptors in the skin which is responsible for the well-known cooling sensation that provokes when inhaled, taken orally or applied to the skin [2]. Similar to capsaicin, responsible for the spiciness of hot peppers (which stimulates heat sensors, without causing a change in body temperature) Menthol has analgesic properties that are mediated through a selective activation of κ-opioid receptors [3]. Menthol also enhances the efficacy of ibuprofen in topical applications via vasodilatation, which reduces skin barrier function [4].

In high concentration, Methyl salicylate is used as a rubefacient in deep heating liniments (such as Bengay) to treat joint and muscular pain. Randomized double blind trial reviews report evidence of its effectiveness that is weak, but stronger for acute pain than chronic pain, and that effectiveness may be due entirely to counter-irritation. However in the body, it metabolizes into salicylates [5].

The main chemical components of clove oil are eugenol, eugenol acetate, iso-eugenol and caryophyllene (terpenes). Eugenol may reduce the ability to feel and react to painful stimulation. Therefore, use of clove products on the skin with other numbing or pain-reducing products such as lidocaine / prilocaine cream, theoretically it may increase effects. FT-IR and partitioning studies reveal that the enhancement in the permeability coefficient of drug by Eugenol is due to lipid extraction and improvement in the partitioning of the drug to the systemic circulation [6-8]

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MATERIALS AND METHODS

MATERIALS

Carbopol 971 was gifted from Corel Pharma Chem, Ahmedabad. Menthol and Methyl Salicylate were obtained from Chinubhai Motilal Saraiya, Ahmedabad. All other ingredients used in the study were of analytical grade.

METHODS

Preparation of Ointment

5 Ointment bases were selected as per their performance properties for topical delivery. They are prepared as per the formula mentioned in table: 1.

Aqueous phase (distilled water at 60°-70°C) was taken in a 250 ml glass beaker with continuous stirring by using propeller stirrer. An accurate quantity of water-soluble material was dispersed when vortex is formed. Oils and other oil soluble material were melted at 60°-70°C.

Table 1: Base formulation – A to E

INGREDIENTS	AMOUNT (%)				
	A	B	C	D	E
Bees Wax		8			
Borax		0.5			
Carbomer 971				1	
Castor Oil					5
Cetomacrogol			6		
Cetyl Alcohol	0.5	1	1.5		
Dimethicone				1	
Glycerin	18		3	1.5	
Lanolin			1		
Liquid Paraffin		50			15
Methyl Paraben	0.2	0.2	0.2	0.2	
Paraffin Wax		12			
Polyethelene Glycol 4000					30
Polyethelene Glycol 400					50
Potassium Hydroxide	0.52				
Sodium Lauryl Sulphate				0.5	
Stearic Acid			6		
Stearic Acid	18				
Triethanolamine			4.5	Q.s.	
Purified Water	Q.s to 100	Q.s to 100	Q.s to 100	Q.s to 100	

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Both the phases were mixed using propeller stirrer by maintaining the temperature. 5% Menthol was dissolved in 15% Methyl Salicylate in separate container and clear solution was obtained. Clove oil was added up to 1 % in the respective formulation. This clear solution was added to biphasic mixture of oil and water when it was hot in the propeller stirrer. It was allowed to cool at room temperature until uniform consistency obtained. The final formulation was pecked in the wide-mouth jar, labelled and evaluated.

Table 2: Formulation code

Formulation Code	Base code	Amount (%)		
		Menthol	Methyl salicylate	Clove oil
I	A	5 %	15 %	-
II	A	5 %	15 %	1 %
III	B	5 %	15 %	-
IV	B	5 %	15 %	1 %
V	C	5 %	15 %	-
VI	C	5 %	15 %	1 %
VII	D	5 %	15 %	-
VIII	D	5 %	15 %	1 %
IX	E	5 %	15 %	-
X	E	5 %	15 %	1 %

EVALUATION OF OINTMENTS [9]

Organoleptic Parameters

Herbal ointment formulations were evaluated based on their 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. It should penetrate through the skin.

pH

10% W/V homogenous solution of ointment was prepared and then pH was calculated by pH meter.

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.

Cooling effect

Cooling effect was determined manually.

Stability study

The optimized formulations along with marketed formulation were evaluated for their stability at an ambient condition of pressure and temperature for two weeks. Formulations were observed for phase separation and particle agglomeration.

Pharmacological screenings by rat paw edema method

Animal study was performed on the developed herbal ointment formulations along with marketed formulation. The animal experiments were performed according to CPCSEA guidelines and after the approval from Institutional Animal Ethics Committee (I.A.E.C.), PROJECT NO. KB/11/227, K. B. Institute of pharmaceutical education and research (KBIPER), Gandhinagar, Gujarat, India. Experiments were conducted in accordance with the standard guidelines. The detailed procedure is discussed as below.

Animal used

Albino rats (Wistar strain) of either sex (150- 180 g) were obtained from the animal house of K. B. Institute of pharmaceutical education and research, gandhinagar, Gujarat. Animals were kept in animal caging system (four rats per cage on beds of sawdust) under the laboratory conditions (25 ± 2°C, 12 h light). They were provided with animal feed pellets manufactured by Hindustan Lever (India) Ltd. Mumbai. Animals were randomly selected for different experimental groups and used for the in vivo determination of anti-inflammatory activity. During the course of the experiment the animal behavior was normal.

Drug/Formulation

Developed Ointment formulations, market preparation (ointment)

Experimental Method

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 hour, 4 hour by using a plethysmometer (Model 7150, UGO Basile, Italy). Edema was expressed as the mean increase in paw volume relative to control. The percentage inhibition of edema was calculated by the following equation:

$$\% \text{ inhibition of edema} = 100\,[1-(Vt/Vc)]$$

Where, Vc = edema volume in the control
Vt = edema volume in test.

RESULTS AND DISCUSSION

As mentioned in table no. 2 different ointment formulations were prepared by using five ointment bases, 5 % Menthol, 5 % Methyl salicylate and 1 % Clove oil. Among them five ointment formulations (formulation code II, IV, VI, VIII, X) contained 1 % Clove oil.

Table 3 showed the comparative evaluation of the prepared ointments. pH, spreadability, consistency, washability, film formation, irritation, cooling effect and Avg. globule size were evaluated for all the ten ointment formulations. Alongside, stability study was performed and finally rat paw edema method was carried out for the Anti-arthritic (anti-inflammatory) activity. Nine ointments were found to be stable at ambient condition, expect the ointment base D was found to be incompatible with clove oil. As indicated in table 3, the ointment base E (formulation ointment – IX and X) provide good physical properties as well as good skin feeling effect.

Comparison of the market ointment preparation (MOOV and FAST RELIEF) was performed with the developed ointments. Table 4 showed the higher % inhibition of rat paw edema in ointment base E (formulation code IX and X) and it is quite identical with the market preparation. Onset of action and duration of action could be determined by the table 4.
Comparison of formulations (e.g. formulation code I-II, III-IV, V-VI, VII-VIII, IX and X) explained that the presence of Clove oil (1 %) showed better inhibition of paw edema and that confirmed the activity of Clove oil as a penetration enhancer.

CONCLUSION

The ointments prepared by using 5 % menthol and 15 % methyl salicylate as an Active, showed similar effectiveness as the market product did. The addition of clove oil (1%) showed better inhibition of the inflammation with compared to the normal ointment. The Ointments provided approx. 35 % of inhibition and that seemed to be the evidence for the anti-inflammatory activity of the ointment. Water miscible base worked as the best carrier for the drug in concern with stability as well as for the anti-inflammatory activity of the ointment.

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Table 3: Evaluation parameters of developed Ointment formulations

Formulation Code	pH	Spreadability	Consistency	Washability	Film Formation	Irritation	Cooling	Avg. Globule Size (μ)
I	7.4	++*	++	+	Greasy	No	Yes	55.4
II	7.6	++	++	+	Greasy	No	Yes	56.8
III	6.8	++	++	+	Poor	No	Yes	59.6
IV	6.8	+++	++	+	Poor	No	Yes	61.9
V	6.9	++	++	++	Good	No	Yes	65.1
VI	6.4	++	++	++	Good	No	Yes	66.7
VII	7.2	+++	++	++	Good	No	Yes	38.5
VIII	7.3	--	--	--	--	No	No	41.9
IX	7.3	+++	+++	+++	Conti.	No	Yes	39.4
X	7.1	+++	+++	+++	Conti.	No	Yes	42.5

*Indicated Good: +++, Moderate: ++, Poor: +

Table 4: Percent Inhibition on carrageenan induced Rat paw edema

Formulation	% Inhibition of edema with Time (hr)				
Batch code	**15 min**	**30 min**	**1 hr**	**2 hr**	**4 hr**
I	9.24	11.5	14.25	17.12	18.92
II	12.83	15.21	17.8	19.72	20.26
III	13.31	14.55	16.72	19.92	22.71
IV	15	18.3	19.5	21.13	25.5
V	13.61	15.62	20.97	24.2	26.11
VI	16.22	19.03	22.18	25.67	27.47
VII	20.6	22.52	27.8	29.92	30.11
VIII	21.2	24.56	29.33	31.5	39.54
IX	24.67	28.45	33.49	38.92	41.23
X	25.82	32.91	38.28	40.65	
M1*	18.25	22.98	31.14	39.43	42.68
M2*	28.51	32.1	41.23	37.92	28.12

*= Marketed formulation (M1 – MOOV, M2 - FAST RELIEF)

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