WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 5, 1940-1949. Review Article ISSN 2277– 7105

AN ADVANCE REVIEW ON SALICYLIC ACID OINTMENT FOR TREATMENT OF ACNE

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Article Received on
15 March 2020,
Revised on 05 April 2020,
Accepted on 26 April 2020
DOI: 10.20959/wjpr20205-17466

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ABSTRACT

Main objective of this study was to formulate the ointment with different ointment bases for topical delivery of water insoluble anti acne agent salicylic acid to enhance the solubility penetration through skin for its activity. The medicated ointment was prepared by using incorporation method in which the active drug has been incorporated in ointment base for topical delivery via skin. To assess the efficacy of the formulation assay, drug release, diffusivity, viscosity, rheology, spreadability, permeability and other physical characterstics were evaluated. Topical ointments provides a suitable delivery system for drug which are water insoluble and having low solubility or having poor penetration efficiency. This review focuses on research till now done on anti acne ointment an detailed study over it.

KEYWORDS: Anti acne ointment, Salicylic acid, Solubility, Penetration.

INTRODUCTION

An ointment is a homogeneous, viscous, semi-solid preparation, most commonly a greasy, thick oil (oil 80% - water 20%) with a high viscosity, that is intended for external application to the skin or mucous membranes. Ointments have a water number that defines the maximum amount of water that it can contain. They are used as emollients or for the application of active ingredients to the skin for protective, therapeutic, or prophylactic purposes and where a degree of occlusion is desired. Ointments are used topically on a variety of body surfaces. These include the skin and the mucous membranes of the eye (an *eye ointment*), chest, vulva, anus, and nose. An ointment may or may not be medicated. Ointments are usually very moisturizing, and good for dry skin.[1][2] They have a low risk of sensitization due to having few ingredients beyond the base oil or fat, and low irritation risk.

Salicylic acid is a beta hydroxy acid and a very commonly used OTC drug for treatment of acne in various formulations such as facewash, face creams, lotions and ointments. It is a keratolytic which acts by dissolving the bonds that holds the dead skin cells together and helps them to shed away more efficiently and it works best for mild pimples and comedonal acne. A concentration ranging from 0.5 -6% of salicylic acid can be used while formulating a medicated ointment for acne and pimples.[14]

Modern day ointments deserves too serve the purpose of emollient as well as protectives but they also carry drug to the blood stream.[4][7] Accordingly they are known as

a) Epidermatic - meant for action on epidermis.
b) Endodermatic – meant for actions on deeper layers of cutaneous tissues.
c) Diadermic – meant to penetrate deep and release medicaments in body fluids.

An ointment may or maynot be medicated. Medicated ointment contains a medicament dissolved, suspended or emulsified in the base. Ointments are used topically for several purposes, e.g. as protectant, antiseptics, emollients, keratolytics and astringents.

Charactrestics of an ideal ointment

1. It should be stable.
2. The base used should not interfere with the active ingredient.
3. The drug used should be uniformly distributed throughout.
4. The formulation prepared should be free from greetiness and must be smooth.[10]

Advantages of ointment

1. They avoid first pass metabolism of drug.
2. Suitable for incorporating bitter tasting drugs.[6]
3. Better patient compliance as easily acceptable by pediatrics and geriatrics.
4. Provide target delivery of drug to a specific site.
5. Comparitively more stable chemically.[6]

Disadvantages of ointment

1. Due to oily preparation these formulations produce stains.
2. On application it may cause itching or might cause contamination.
3. Physico-chemically less stable than solid dosage form.
4. Bulky to handle.
5. Phase separation or cracking may occur.

Ointment Bases

Ointment bases is basically a vehicle into which an active ingredient in the form of solution, suspension or dispersion may be incorporated.[3][5]

Ideal properties of ointment base

The ointments must possess the following ideal characterstics -

1. Must be non greasy.
2. Must be inert.
3. A low index of irritancy.
4. Low sensitization index.
5. Compatible with active agent used.

Classification of ointments

The ointment bases are usually of five types on the basis of their physical composition -

a) Oleaginous bases - These bases consists of oils and fats. The most important are the hydrocarbons like petrolactum, paraffins and mineral oils. The combination of these materials can produce a product of desired melting point and viscosity. They are highly compatible, occlusive and emollients.

b) Absorption bases – The term absorption base is used to denote the water absorbing or emulsifying property of these bases and not to describe their action on the skin. These bases are generally anhydrous, water insoluble and water unwashable. Examples are wool fat, hydrophilic petrolactum.

c) Water removable bases – They are oil in water emulsion that are capable of being washed from skin or clothing with water. For this reason they are frequently referred as water washable ointment base.

d) Water soluble bases – They contain only the water soluble ingredients and not the fats or other greasy substances hence are alsoncalled greaseless bases. Examples are carbowaxes and macrogols.

Formulation Consideration

Besides base and medicaments the ointment may contain one or other groups of additives.

a) Preservatives – The microbial compounds and their quantities should be carefully decided upon if the same are being used to prevent contamination, deterioration or spoilage of ointment bases by bacteria and fungi. Examples are sorbic acid, calcium benzoate.

b) **Antioxidants** – Anti oxidants should be included whenever there is possibility of oxidative degradation of bases. The concentration of anti oxidants depends upon their partition coefficient between the aqueous and oil phase of both the phases. Examples are retinol, niacinamide, polyphenols.

c) **Chelating agents** – Whenever it is anticipated that traces of metallic ions are likely to catalyze oxidative degradation small amounts of these agents must be added. Examples are citric acid, maleic acid, phosphoric acid.

d) **Perfumes –** Most ointment bases these days have a pleasant smell imparted by incorporation of select blends.

Preparation of ointments

Ointments can be prepared either by mechanical incorporation or by fusion methods. Irrespective of the methods employed for preparation, ointments should be smooth and free from granular or gritty particles. The method used primarily depends on type of ingredients used.

a) Incorporation Method

By the incorporation method, the components are mixed until a uniform preparation is attained, on a small scale the pharmacist may mix the components using a mortar and pestle or a spatula and slab.

Incorporation of solids

When preparing an ointment by spatulation, the pharmacist works the ointment with a stainless spatula having a long, broad blade. If the components of an ointment are reactive with the metals of the spatula. The ointment base is placed on one side and the powdered components previously reduced to fine powders on the other side. A small portion is mixed with a portion of the base until uniform mixture is obtained. The process is continued until all portions of the powder and the base are combined and thoroughly and uniformly blended.

Incorporation of liquids

Liquid substances or solutions of drugs are added to an ointment according to ointment base's capacity to accept the volume required. For example, only small amount of an aqueous solution may be incorporated into an oleaginous ointment, whereas hydrophilic ointment bases readily accept aqueous solutions.

b) Fusion Method

By the fusion method all or some of the components of an ointment are combined by being melted together and cooled with constant stirring until congealed. Components not melted are added to the congealing mixture as it is being cooled and stirred. Naturally heat labile substances and any volatile components are added last when the temperature of the mixture is low enough not to cause decomposition or volatilization of the components. On a small scale the fusion process is conducted in a porcelain dish or glass container. In the preparation of ointments having an emulsion base the method of manufacture involves both a melting and an emulsification process. The water immiscible components such as oils and waxes are melted together in a steam bath to about 70-75^{0}C and an aqueous solution of the heat stable water soluble components is prepared and heated to the same same temperature, then the aqueous solution is slowly added with mechanical stirring to the melted oleaginous mixture. The temperature is maintained for 5-10 minutes and the mixture is slowly cooled with the stirring continued until congealed.

Evaluation of ointments[9][16]

i) Physical Examination

The Prepared ointment formulations were inspected visually for their colour, homogeneity, consistency.

ii) Determination of pH

2.5gm Ointment sample was taken in 100 ml dry beaker, 50 ml water was added to it. Beaker was heated on water bath maintained at about 60ºC to 70ºC for 10 minutes, cooled to room temperature, and then centrifuged at 3000 rpm for 10 minutes. The pH of water extract was measured by using pH meter. The pH measurements were done by using a digital type pH meter by dipping the glass electrode into the ointment formulation.

iii) Percentage Yield

The empty container was Weighed in which the gel formulation was stored then again the container was weighed with gel formulation. Then subtracted the empty container weighed with the container with gel formulation then it gives the practical yield. Then the percentage yield was calculated by the formula.

$$\text{Percentage yield} = \frac{\text{Practical yield}}{\text{Theoretical yield}} \times 100$$

iv) Drug content

Weighed 10 gm of each gel formulation were transferred in 250 ml of the volumetric flask containing 20 ml of alcohol and stirred for 30 min. The volume was made up to 100 ml and filtered. 1 ml of the above solution was further diluted to 10 ml with alcohol and again 1 ml of the above solution was further diluted to 10 ml with alcohol. The absorbance of the solution was measured spectrophotometrically at >290 nm. Drug content was calculated by the following formula

$$\text{Drug content} = \frac{\text{Absorbance}}{\text{Slope}} \times \text{Dilution factor} \times \frac{1}{1000}$$

v) Determination of pH

Weighed 50 gm of each gel formulation were transferred in 10 ml of the beaker and measured it by using the digital pH meter. pH of the topical gel formulation should be between 3–9 to treat the skin infections.

vi) Spreadability

It indicates the extent of the area to which gel readily spreads on application to the skin or affected part. The therapeutic potency also depends upon spreading value. The time in sec taken by two slides to slip off from ointment which is placed in between the slides under the direction of certain load is expressed as spreadability. Lesser the time taken for the separation of two slides, better the spreadability. The following formula is used to calculate the spreadability:

$$\text{Spreadability (S)} = M \times L / T$$

Where,

M = weight tied to upper slide

L = length of glass slides

T = time taken to separate the slides

vii) Extrudability

The ointment formulations were filled into a collapsible metal tube or aluminium collapsible tube. The tube was pressed to extrude the material and the extrudability of the formulation was checked. The formulations are fill in the collapsible tubes, after it was set in the container. Extrudability is determine in terms of weight in gm required to extrude a 0.5 cm ribbon of ointment in 10 second.

viii) Viscosity estimation

The viscosity of ointment was determined by using a Brookfield viscometer DVII model with a T-Bar spindle in combination with a helipath stand.

a) **Selection of spindle**: Spindle T 95 was used for the measurement of viscosity of all the ointments.
b) **Sample container size**: The viscosity was measured using 50 gm of ointment filled in a 100 ml beaker.
c) **Spindle immersion**: The T-bar spindle (T95) was lowered perpendicular in the centre taking care that spindle does not touch the bottom of the jar.
d) **Measurement of viscosity**: The T-bar spindle (T95) was used for determining the viscosity of the ointments. The factors like temperature, pressure and sample size etc. Which affect the viscosity was maintained during the process. The helipath T-bar spindle was moved up and down giving viscosities at a number of points along the path. The torque reading was always greater than 10%. The average of three readings taken in one minute was noted as the viscosity of ointments.

***x) In vitro* diffusion study**

The abdominal skin of Albino mice, weighing 20–25 gm of 8–10 w old was shaved using hand razor and clean the skin with hot water cotton swab. 5 gm of ointment was applied uniformly to the skin. The skin was mounted between the compartments of the Frantz diffusion cell with stratum corneum facing the donor compartment. Reservoir compartment was filled with 100 ml phosphate buffer of pH 6.8. The study was carried out at 37±1 °C and the speed was adjusted until the vortex touches the skin and it carried out for 4½ h. 5 ml of the sample was withdrawn from the reservoir compartment at 30 min interval and absorbance was measured spectrophotometrically at 260 nm. Each time the reservoir compartment was replenished with the 5 ml volume of phosphate buffer pH 6.8 solution to maintain a constant volume.

xi) Skin irritation study

For skin irritation study, Guinea pigs (400-500g; either sex) were used. The animals were maintained on the standard animal feed and had free access to water. The animals were kept under standard conditions. Hair was shaved from the back. Five ml of each sample was withdrawn periodically at 1,2,3,4,5,6,7 and 8h and each sample was replaced with an equal volume of fresh dissolution medium. Then analyzed the samples for drug content by using

phosphate buffer as guinea pigs and an area of 4 cm was marked blank on both the sides, one side served as control while the other side was test. The ointment was applied (500 mg/ guinea pig) twice a day for 7 days and the site was observed for any sensitivity and the reaction if any.

CONCLUSION

Ointments are getting more popular nowadays because they are more stable and also can provide controlled release than other semisolid preparations like creams, gels, pastes, etc. The ointment formulation can provide better absorption characteristics and hence increase the bioavailability of the drug. A thorough investigation into the stability characteristics of the ointment formulation over an extended period of time may provide scope for its therapeutic use for patients. Since the polymer is water soluble; consequently, it forms a water washable ointment and has wider prospects to be used as a topical drug delivery dosage form. The principal advantage of topical drug delivery lies in targeting the drug action directly to the site of disorder by allowing accumulation of high local drug concentration within the tissue and around its vicinity for enhanced drug action this is more effective when drugs with short biological half-life, narrow therapeutic window are applied with topical route. The clinical evidence shows that topical ointment is a safe and effective treatment choice for use in the management of skin related diseases. Various formulation were developed by using a suitable ointment base. Developed formulations of salicylic acid were evaluated for the physiochemical parameters such as percentage yield, drug content, pH, viscosity, spreadability, extrudability, *in vitro* drug diffusion. Viscosity studies of various formulations revealed that some formulation was better to compare to others. From among all the developed formulation, some formulation shows better drug diffusion, did good Rheological properties. pH of the some formulation is sufficient enough to treat the skin infections. Hence formulation some should be further developed for scale-up to industrial production.

ACKNOWLEDGEMENT

The author expresses gratitude to GRD (PG) IMT and Director of pharmacy N.G. Raghavendra Rao and the concerned guide Yogita Tyagi for their kind support in providing all facilities related to this manuscript.

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