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A COMPERHENSIVE REVIEW ON PHARMACEUTICAL OINTMENT

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Abstract:

Pharmaceutical ointments are the semisolid dosage form of medicaments which is totally W/O or O/ W type of medicaments. These preparations serve as a carrier for drugs. Ointment can adhere to the application surface for long period of time before they are washed off with a tap water. These property of ointment helps for prolong drug delivery at the site externally apply on skin. Ointments may be medicated or non-medicated. They generally contain medicaments and are intended to be applied externally to the body or to the mucous membrane. Many medicaments meant for topical application to intact or broken skin or to mucous membranes, have been presented in the form of semisolid consistency variously designated as ointments, creams, salves, pastes etc used mainly as protective or emollient for the skin. The first step towards this goal is the screening of plants used in popular medicine. Along with other dosage forms, herbal drugs are also formulated in the form of ointment.

Keywords: Ointment method, Ointment bases, Iodine ointment, semisolid, Cetostearyl alcohol.

INTRODUCTION

Herbal medicines are being used by about 80% of the world population primarily in the developing countries for primary health care.[1] They have stood the test of time for their safety, efficacy, cultural acceptability and lesser side effects. Ancient literature also mentions herbal medicines for age-related diseases namely memory loss, osteoporosis, osteoarthritis, diabetes, immune and liver disorders, etc.[2] for which no modern medicine or only palliative therapy is available.[3] The chemical constituents present in them are a part of the physiological functions of living flora and hence they are believed to have better compatibility with the human body[4]. There are over 1.5 million practitioners of traditional medicinal system using medicinal plants in preventive, promotional and curative applications.[5] Medicinal plants have attracted the attention of not only professionals

from various systems of medicine, but also the scientific communities belonging to different disciplines, plants are promising source of herbal formulation[6]. The use of herbal drugs due to toxicity and side effects of allopathic medicines, has led to rapid increase in the number of herbal drug manufacturers.[7] For the past few decades, herbal drugs have been more and more consumed by the people with no prescription.[8] These drugs have survived real world testing and thousands of years of human testing. Some drugs have been discontinued due to their toxicity, while others have been modified or combined with additional herbs to counterbalance side effects.[9]

Advantages of Herbal Drugs

1. High Low/Minimum cost
2. Complete accessibility
3. Enhanced tolerance

Role of herbals in modern human era

Many of the currently available to physicians have a long history of use as herbal remedies.[10] The who estimate that 80 percent of the world's population presently use herbal medicine for some aspect of primary health care .in fact ,according to the world health organization ,approximately 25% of modern drugs used in the united states have been derived from plants.[11] Among the 120 active compounds currently isolated from the higher plants and widely used in modern medicine today, 80 percent shows a positive correlation between their modern therapeutic use and the traditional use of the plants from which they are derived.[12]

1. More than two thirds of the worlds plant species –at least 35,000 of which are estimated to have medicinal value –come from the developing countries.[13]

2. At least 7,000 medicinal compounds in the modern pharmacopoeia are derived from plats The Challenges in Herbal Medicines[14]

A key challenge is to objectively assess conflicting toxicological, epidemiological, and other data and the verification of herbal materials used. The following key issues remain.[15]

1. Management within ranges of risk
2. Communication of uncertainty
3. Pharmacological, toxicological, and clinical documentation
4. Pharmacovigilance
5. Understanding why addition of harmful additives works
6. evaluating "drug" interactions
7. Constraints with clinical trials and people available
8. Standardization

9. Safety, and efficacy assessment

OINTMENTS

Semisolid dosage forms such as ointments may be used for topical application to the skin,[16] placement on the surface of the eye, or for nasal, vaginal, or rectal use for medicinal or protective activities or cosmetic purposes.[17] These preparations are used for the limited effects they have on the skin or mucous membrane at the moment of application due to drug penetration, and they are why they are used.[18] In the treatment of cutaneous illnesses, these devices are intended to deliver the medication directly into the skin, with the skin serving as the target organ.[19] Emulsions of oil and water are used to create the semi-solid substance known as an ointment.[20] Both oil-in-water (O/W) and water-in-oil (W/O) ointments are composed of very small droplets of oil and water that are distributed uniformly across a continuous oily or watery phase, respectively.[21] Ointments may either be oil-in-water or water-in-oil, and this distinction is based on how the oil is distributed throughout the product.[22] Because they are less oily and can be removed with water more readily, ointments that include oil and water are more pleasant to use and are appropriate for cosmetic use.[23] It is more difficult to work with water-in-oil ointments, but because many of the medications that are included in ointments are hydrophobic, they will be released more easily from a water-in-oil cream than from an oil-in-water cream.[24] Water-in-oil ointments have the disadvantage of being less stable.[25] Because they create an oily barrier, water-in-oil ointments are also more moisturizing.[26] This barrier helps to minimize the amount of water that is lost from the stratum corneum, which is the skin's outermost layer.[27] Traditional medical practices are being championed by both the World Health Organization (WHO) and the United States of America due to the fact that they are less costly, readily accessible, and comprehensive, particularly in poor nations. In addition to this, it is a fact that just eight percent of the world's population receives the majority of their main medical treatment from plants.[28] The significance of traditional medicine has been acknowledged on a global scale, especially in affluent nations; as a result, there are now treatment techniques, protocols, and standards in place for ethnomedicine.[29] There are many different signs and symptoms that may be caused by skin illnesses, and in many cases, the therapy must be maintained for an extended period of time. It is necessary to have a herbal skin cream that is both safe and effective in order to cure a variety of skin conditions, including wounds, acne vulgaris, fissures, psoriasis, and other sorts of skin illnesses. Although there are many different kinds of cream that are regarded for wound healing, it still seems that they have a limited capacity for the pace of tissue regeneration. As a result, after doing an in-depth study into the pathophysiology of wound healing and the many conventional and alternative treatments available. Homeopathic systems of medicine all provide a significant amount of information pertaining to skin care. In this day and age, the expertise and experience gained through the use of herbs is being combined with cutting-edge cosmetic technology in order to provide a product that is not only secure and efficient but also acceptable to a greater number of individuals.[30]

DEVELOPMENT OF HERBAL OINTMENT

According to survey report by WHO, about 25 per cent of prescribed human medicines are derived from plants and 80 per cent people still depend on traditional system of medicines. The herbal wealth of India and the knowledge of their medicinal properties have a long tradition, as referred in Rig veda and other ancient literature. The topography of India in the tropical belt with its varied climatic zones made it a vast storehouse of medicinal plants.[31] The quality assessment of herbal formulations is of paramount importance in order to justify their acceptability in modern system of medicine. One of the major problems faced by the herbal industry is the unavailability of rigid quality control profiles for herbal materials and their formulations. Regulatory bodies have laid down the standardization procedures and specifications for Ayurvedic preparations.[32] The World Health Organization (WHO) has appreciated the importance of medicinal plants for public health care in developing nations and has evolved guidelines to support the member states in their efforts to formulate national policies on traditional medicine and to study their potential usefulness including evaluation, safety, and efficacy.[33]

PROBLEM IN HAND

Aloevera gel has higher antibacterial efficacy towards Streptococcus mitis. Research through Hayes, Lichen and Choonhakarn et al. Confirmed that Aloe vera juice and gel are substantially greater green than the placebo inside the therapy of oral lichen planus.[34] Aloe gel became proven to be greater powerful to herpetic virus lesions if applied directly.[35] Acemannan hydrogel has been shown to hurry up the recovery process for aphthous ulcers and lessen their pain.[36] Using aloe vera gel as a topical remedy for gum tissue and surgical incisions, as well as regions irritated by means of toothbrush bristles, dental floss, or meals debris, has lengthy been a preferred coaching.[37] Aloe vera helps dry sockets heal faster and prevents them from forming within the first location.[38] Various concentrations of Aloe vera were proven to lessen the recovery duration of wounds.[39] Three levels of wound recuperation are concerned. Inflammation, hyperemia, and leukocyte permeation occur inside the preliminary segment. Dead tissue is eliminated inside the 2nd stage, and new tissue is generated inside the 1/3 degree, which includes regeneration of the epithelium and the improvement of fibrous tissue.[40] Aloe vera is hailed as a "natural healer" for its potential to hurry up the recovery system and reduce inflammation in first- and second-level burns. The wound-restoration procedure is elevated via using aloe gel.[42] Additionally, Aloe

vera's antibacterial, antiseptic, and anti-viral characteristics resource in the recuperation method. Microorganisms are slowed down by means of using Aloe juice, which boosts immunity and speeds up cellular recovery. It additionally reduces shingles ache, reduces psoriasis signs and symptoms, and alleviates heartburns and ulcers with its soothing homes.[43] The 99 percentage water content of aloe gel prevents wound dryness and promotes epithelial cellular migration. Catechol amines, which inhibit wound restoration, are blocked through aloe vera, which stimulates epithelization and complements vascularization, allowing lifeless tissue to be replaced and wounds to heal. Anti-wrinkle houses are attributed to Aloe polysaccharides and boom hormone gibberellins.[44] A kind of muco-polysaccharides (MPS) also are thought to have a position in Aloe vera's capacity to heal. Mannose-6-phosphate, glucomannan, and gibberellin, a boom hormone, have all been implicated in wound recuperation. Some of Aloe vera's amino acids and enzymes are taken into consideration to help regenerate scar tissue with the aid of speeding up the advent of latest pores and skin cells.[45] Anti-growing old and anti-wrinkle protein collagen can also be advanced by means of aloe's ability to stimulate macrophage cytokine production. Additionally, acemannan has been shown to stimulate macrophages.[46] When carried out to wounds, the Aloe vera anthraquinones within the plant assist to speed up the recovery method by means of destroying pus and lifeless cells.[47] Aloe vera can be used to deal with small wounds, insect stings, welts, poison ivy, and eczema, amongst different conditions. Using aloe vera gel may also help preserve the skin moisturised due to its humectant properties.[48]

Preparation of ointment

(a) Uniform throughout i.e. it contains no lumps of separated high melting point ingredients of the base, there is no tendency for liquid constituents to separate insoluble powders are evenly dispersed.[49]

(b) Free from grittiness, i.e. insoluble powders are finely subdivided and large lumps of particles are absent. Methods of preparation must satisfy these criteria.

Two mixing techniques are frequently used in making ointments:

1. Fusion, in which ingredients are melted together and stirred to ensure homogeneity.

2. Trituration, in which finely subdivided insoluble medicaments are evenly distributed by grinding with a small amount of the base or one of its ingredients followed by dilution with gradually increasing amounts of the base.[50]

When an ointment base contains several solid ingredients such as white beeswax, cetyl alcohol, stearyl alcohol, stearic acid, hard paraffin, etc. as components of the base, it is required to melt them.[51]

The melting can be done in two methods

Method-I

The components are melted in the decreasing order of their melting point i.e. the higher M.P. substance should be melted first, the substances with the next melting point and so on. The medicament is added slowly in the melted ingredients and stirred thoroughly until the mass cools down and a homogeneous product is formed.[52]

Advantage:

This will avoid over-heating of substances having a low melting point.

Method-II

All the components are taken in a subdivided state and melted together.

Advantage:

The maximum temperature reached is lower than Method-I, and less time was taken possibly due to the solvent action of the lower melting point substances on the rest of the ingredients.[53]

Cautions:

(i) Melting time is shortened by grating waxy components (i.e. beeswax, wool alcohols, hard-paraffin, higher fatty alcohols and emulsifying waxes) by stirring during melting and by lowering the dish as far as possible into the water bath so that the maximum surface area is heated.[54]

(ii) The surface of some ingredients discolours due to oxidation e.g. wool fats and wool alcohols and these discoloured layers should be removed before use.[55]

(iii) After melting, the ingredients should be stirred until the ointment is cool, taking care not to cause localized cooling, e.g. by using a cold spatula or stirrer, placing the dish on a cold surface (e.g. a plastic benchtop) or transferring to a cold container before the ointment has fully set. If these precautions are ignored, hard lumps may separate.[56]

(iv) Vigorous-stirring, after the ointment has begun to thicken, causes excessive aeration and should be avoided.[57]

(v) Because of their greasy nature, many constituents of ointment bases pick up dirt during storage, which can be seen after melting. This is removed from the melt by allowing it to sediment and decanting the supernatant, or by passage through muslin supported by a warm strainer. In both instances, the clarified liquid is collected in another hot basin.[58]

(vi) If the product is granular after cooling, due to separation of high M.P. constituents, it should be remelted, using the minimum of heat, and again stirred and cooled.[59]

Example:

(i) Simple ointment B.P. contains

Wool fat -50g

Hard paraffin -50g

Cetostearyl alcohol -50g

White soft paraffin -850g

Type of preparation: Absorption ointment base.

Procedure:

Hard paraffin and Cetostearyl alcohol on water-bath. Wool fat and white soft paraffin are mixed and stirred until all the ingredients are melted. If required decanted or strained and stirred until cold and packed in a suitable container.[60]

(ii) Paraffin ointment base

Type of preparation: Hydrocarbon ointment base.

(iii) Wool alcohols ointment B.P.

Type of preparation: Absorption base.

(iv) Emulsifying ointment B.P.

Type of preparation: Water-miscible ointment base.

(v) Macrogol ointment B.P.C

Type of preparation: Water-soluble ointment base.

Formula: Macrogol 4000

Liquid Macrogol 300

Method: Macrogol 4000 is melted and previously warmed liquid macrogol 300 is added. Stirred until cool.

Preparation of Ointments by Trituration:

This method is applicable in the base of a liquid present in a small amount.

(I)Solids are finely powdered are passed through a sieve (# 250, # 180, #125).

(ii) The powder is taken on an ointment-slab and triturated with a small amount of the base. A steel spatula with a long, broad blade is used.[62] To this additional quantities of the base are incorporated and triturated until the medicament is mixed with the base.[63]

(iii) Finally, liquid ingredients are incorporated. To avoid loss from splashing, a small volume of liquid is poured into a depression in the ointment and thoroughly. Incorporated before more is added in the same way. Splashing is more easily controlled in a mortar than on a tile.

Examples

(i) Whitfield ointment (Compound benzoic acid ointment B.P.C.)

Formula:

Benzoic acid, in fine powder – 6 gm

Salicylic acid, in fine powder – 3gm

Emulsifying ointment – 91gm

Method: Benzoic acid and salicylic acid are sieved through No. 180 sieves. They are mixed on the tile with a small amount of base and levigated until smooth and dilute gradually.

(ii) Sulphur ointment I.P.

Sublimed sulphur – 10 g

Simple ointment – 90 g

Prepare an ointment.

Method: Sublimed sulphur is sieved through no. 180 sieves. Then sublimed sulphur is triturated with a small amount of simple ointment. Then the remaining amount of simple ointment is added and the mixture is levigated until a smooth and homogenous mass is obtained.

Preparation of Ointments by Chemical Reaction:

Chemical reactions were involved in the preparation of several famous ointments of the past, e.g. Strong Mercuric Nitrate Ointment of the 1959 B.P.C.

An ointment containing free iodine

Iodine is only slightly soluble in most fats and oils. Lodine is readily soluble in a concentrated solution of potassium iodide due to the formation of molecular complexes KI-I2, KI-2I2, KI-3I2 etc.

These solutions may be incorporated in absorption-type ointment bases.

Evaluation test for ointment

1 Test of rate of absorption

The ointment should be evaluated for the rate of absorption of drugs into the blood stream in vivo only. The ointment should be applied over a infected area of the skin by rubbing. At regular interval of time serum and urine sample should be analyzed for the quantity of drug absorbed

2. Test of non-irritancy

The bases used in the formulation of ointment may cause irritation or allergic reaction. Non irritancy of preparation is determine by patch test. In this test human volunteers are selected.Definite quantity of ointment is applied under occlusion daily on the back or volar fore arm for some time period. Information is noted on daily basis.

3.Test of rate of penetration

The rate of penetration of semi-solid dosage form is crucial in the onset and duration of action of the drug. Weighed the quantity and applied over the skin for a definite period of time. Then the preparation left over is collected and weighed. The difference between the initial and the final weight and the final weight of the preparation gives the amount of preparation penetrated through the skin and this when divided by the area and the time period of application give the rate of penetration of the preparation. The test should be repeated 2 to 3 times.

4.Test of rate of drug release.

To assess the rate of release of medicament small amount of the ointment can be placed on the surface of nutrient agar contain in a petri dish or alternately in a small cup in the agar surface. If the medicament is bactericidal the agar plate is previously seeded with a suitable organism like staphylococcus aureus. After a suitable period of incubation the zone of inhibition is measured and correlated with the rate of release.

5.Test of rheological properties.

The viscosity of the preparation should be such that the product can be easily optimal from the container and easily applied over the skin. Using cone and plate viscometer the viscosity of the preparation is determine.

6.Test of content uniformity.

The net weight of contents of ten filled ointment containers is determined. The result should match each other and with the labeled quantity.

7. Test of preservative efficacy

Using pour plate technique the number of microorganism initially present in the preparation are determine. Solutions of different samples of preparation are made and mix with tryptone azolectin (TAT) broth separately. All cultures of microorganism are added into each mixture, under aseptic condition. All mixture are incubated .The number of microorganism in each sample are counted on 7th, 14th, 21st and 28th days of inoculation.

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