NEW UNGUENT BASES AND LOTIONS

Formulae and Uses

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FOREWORD

As a dermatologist, the work of Dr. Hoffman has held a special interest for me since much of dermatological therapy is based on administration of various medicaments to the skin. It is, therefore, of obvious importance that the physician should be well informed of the various lotions and unguent vehicles that are available and the properties they possess. Some of these are as follows: compatibility, consistency, release of active ingredients, absence of irritation, ease of removal, and finally esthetic value. It is equally obvious that for the physician alone to be aware of the attributes of an acceptable vehicle for topical medicaments is of little value if the individuals responsible for compounding do not prepare a satisfactory product. This applies to all the professions concerned whether they are in small or large commercial practice.

The original material presented in this volume is noteworthy because of the comprehensiveness with which the work is treated. For the first time, many types of excellent topical preparations have been made available to physicians, pharmacists, and chemists in a book written primarily for those in the dermatological and allied fields. As a ready reference, the advantages offered in the saving of time and effort is indeed commendable. The progress and improvement of vehicles for application to the skin, such as those included in this book, serve as a valuable link in the achievement of more satisfactory therapeutic response. It is also gratifying to observe that the preparations found on these pages are esthetically desirable for all forms of treatment.

The simplicity and scope of material in this book should be of benefit to those whose time and familiarity is, by necessity, limited. The author's wide experience contributes much toward a greater appreciation and understanding of good dermatological unguents and lotions.

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TO MY MOTHER AND FATHER

AUTHOR'S PREFACE

A reference and guide to the more advanced types of unguent bases and lotions has long been needed by the pharmaceutical, medical, and allied professions. The efforts of the author have been rewarded by the satisfaction gained in filling this need.

FOR THE PHARMACIST, this book opens a wide field of reference and application to topical pharmaceutical preparations. From these formulae, he may choose those which are most satisfactory for his needs. He can utilize them as stock vehicles or use the diverse data as a source of information when advising the physician.

FOR THE PHYSICIAN, this book will serve as a ready reference and formula guide to the various classes of dermatological products. Its value as a prescribing aid is enhanced by the description included with each formula. It has also the advantage that it lists specific preparations which can be used for special purposes.

FOR THE PHARMACEUTICAL MANUFACTURER, the formulae in this book can be of great value for commercial product development. The fine appearance, economy, safety, and ease of manufacture of the products listed, will make them especially suitable for pharmaceutical preparations.

FOR THE COSMETIC MANUFACTURER, the versatility and special characteristics of the preparations described in the book present many interesting possibilities for commercial application. They can be combined with all types of perfumes, colors, or other cosmetic materials. As luxury products, these formulations are well chosen because of their attractiveness, effectiveness, safety, economy and ease of manufacture.

FOR USE AS A TEXT, this book is of practical value, because it covers extensively the various classes of emulsified pharmaceutical preparations for topical use. Simple mixtures, solutions, or suspensions are not included. The descriptive material offers useful information to students of pharmacy, medicine, and related fields.

FOR THE LIBRARY, too, this book can be used as a reference, which covers most of the information available in this somewhat limited field. It is a good source for those whose diverse interests touch on this subject. As the lack of compiled material on unguent base and lotion emulsions is sorely evident, the author has taken great pains to put within easy reach the more advanced and practical formulae, methods of preparation, and uses.

In order to make the writing of a book, such as this, worth while, its need and utility must be established. This thought has been considered very carefully and the conclusions evolved are as follows: The information presented here is an application of theory to practice. All of the preparations described have been tried in the laboratory and have been found useful. They can be compounded with a minimum of expenditure in money, time, and effort. Only a few ingredients are necessary for all the classes of vehicles. The differences are created by varying the proportions of the same substances. Additional advantages of these unguent base and lotion formulae are the constant availability and proven safety of the individual ingredients.

The subject matter will satisfy a need for those who are constantly searching for better products. Large sums of money are expended by our drug and cosmetic manufacturing industry on research in order to obtain a desirable characteristic so that a preparation will be, for example, stainless or greaseless. The vehicles listed in this book are attractive, comfortable, versatile, and readily removable.

Every effort has been made to present the subject matter in a clear and concise manner. These new, practical formulae have been developed and tested by the author. This is the only book which is devoted solely to emulsified unguent bases and lotions.

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CHAPTER ONE

INTRODUCTION

The unguent bases and lotions used in dermatological treatment can be quite greaseless, comfortable, and pleasing to the eye. The great advances in the field of emulsions have made possible the creation of stable, pleasant-feeling, nonirritable vehicles. Additional advantages are economy and facility of preparation. There are numerous other advantages, such as ease of removal, absorptive action, wide compatibility, etc., which will be discussed later in more detail.

The new unguent bases and lotions are white and creamlike. They create a sensation of coolness when applied to the skin. This is due to the slow evaporation of water from the emulsion. The evaporation, in turn, permits the escape of heat from the skin surface. The absorptive power of these bases permits the taking up of dermal excretory and secretory products. This property is especially valuable where irritable and purulent fluids are elaborated. The older, more greasy unguents and lotions had a tendency to cause congestion of the skin with subsequent irritation. This discomfort was produced by retarded drainage and restricted evaporation of these excretory products. Thus, the older vehicles encouraged heat retention which contributed to the discomfort.

The properties of a good unguent base or lotion are as follows:

Compatibility with most medicinal agents

Efficient release of therapeutic agents to the skin

Sufficient absorptive action to take up liquids

Nonirritability

Easy removal

Stability

Economy

Good appearance

The new unguent bases have a liquid content of approximately 50 percent. The lotions contain about 90 percent liquid. This consists primarily of water and/or oil. There may, at times, be a variation of this percentage. In the compounding of an unguent base or lotion, the water-soluble substances are dissolved in the aqueous phase and the oil-soluble ingredients are dissolved in the oil phase. The water-soluble and water-dispersible agents most generally used are presented in tables 1 and 2 which list also the common oil-soluble and oil-dispersible ingredients.

To compound a satisfactory unguent base or lotion, it is usually necessary to utilize substances that are both hydrophilic and lipophilic. The hydrophilic agents are associated with the aqueous phase and the lipophilic agents with the oil phase. The two groups, which are normally immiscible, are attracted to each other by surface-active, or emulsifying, agents.

Much credit must be given to colloid chemists for the progress and development of new, effective surface-active agents. Emulsifying agents facilitate the combination of immiscible substances by reducing their surface and interfacial tensions, thus making good, stable emulsions possible. To form emulsions, the ingredients must be reduced to a liquid state. If solids of low melting points are used, heat can readily liquefy them. Surface-active agents are both hydrophilic and lipophilic and thus are able to form a link between water-soluble and oil-soluble substances. The hydrophilic portion of the molecule may be a sulfonate, carboxylate or glycol group. The lipophilic portion may be a long carbon chain, such as a fatty acid group. For example, sodium sulfethyl oleate (a sodium alkyl sulfonate) consists of the following two portions:

$C_{17}H_{33}COO^-$	and	$CH_2CH_2SO_3Na^+$
Lipophilic		Hydrophilic

Surface-active agents are divided into three main classes, depending on the ionic charges they provide. They may be positively charged, negatively charged, or carry no charge at all. The positively charged

surface-active agents are called cationic, those negatively charged are anionic and those without charge are nonionic. The ionic designation denotes the portion of the molecule which conveys the emulsifying properties. For example, the quaternary ammonium salts, such as benzalkonium chloride, are cationic. Soaps and sulfates of long-chain aliphatic alcohols, such as sodium lauryl sulfate, are anionic. Glyceryl esters of fatty acids and sorbitol compounds of fatty acids, such as glyceryl monostearate or sorbitan monooleate, are nonionic.

Surface-active agents produce emulsions of two types: oil-in-water or water-in-oil emulsions. A surface-active agent which exerts greater attraction on one phase than on the other determines the type of emulsion formed. For example, sodium lauryl sulfate is more soluble in the aqueous phase and, therefore, tends to form oil-in-water emulsions. In other words, the choice of the emulsifying agent for producing a specific type of emulsion depends to a great deal on the medium in which the agent is soluble.

The terms *oil-in-water* and *water-in-oil* have a definite meaning in emulsion formulation and their definitions will be given as follows: Oil-in-water signifies that the oil particles are dispersed in the water, so that the water is the external phase and the oil, the internal phase. If the emulsion is of the water-in-oil type, the particles or droplets of the water are dispersed in the oil. In this case, the oil is the external phase and the water, the internal phase. Expressing this another way, the medium in which the surface-active agent is soluble is called the external phase. The physical character of the external phase governs the physical and chemical behavior of the emulsion to a large extent. If water forms the external phase of the unguent base or lotion, the resulting emulsion is washable. The oil-in-water type emulsion can take up additional amounts of water if necessary. Some water-soluble drugs may be incorporated in this emulsion readily without the use of additional liquid. Oily therapeutic agents can also be incorporated due to their attraction to the lipophilic portion of the emulsifying agent. The surface-active agent also tends to reduce the surface tension of added liquids. If the emulsifying agent is cationic, there may be some difficulty when an anionic substance is introduced, resulting in nonuniformity or breaking of the emulsion. In this case, a nonionic surface active agent should be used. When large quantities of water-insoluble (oleaginous) substances are to be incorporated, emulsion bases and lotions of a lower aqueous content, or of the water-in-oil type, should be used.

Water-in-oil unguent bases and lotions are not readily washable. They produce a feeling of oiliness on the skin, but are able to absorb large quantities of aqueous or fatty matter. These emulsions are useful where a substantial proportion of oily emollient is desirable. If cholesterol is combined with this type of vehicle, increased dermal penetration is usually obtained. The water-in-oil emulsion vehicles are employed where more direct contact of oil with the skin is desirable or where washability is not wanted. They exert a greater protective action, but are less comfortable. As a vehicle, they are more efficient for carrying large amounts of oleaginous materials.

There are several ingredients in the new unguent bases and lotions which are suitable for both oil-in-water and water-in-oil emulsions. A good example is stearyl alcohol. This fatty acid derivative is normally oil soluble due to its long carbon chain. It also contains a hydroxyl group which tends to make it water soluble. Thus similar fatty alcohols, such as cetyl alcohol, are also hydrophilic even in water-in-oil emulsions.

Typical representatives of the nonionic emulsifiers are the sorbitol and glyceryl esters of fatty acids. Sorbitol, which is related to the sugars, is a partially dehydrated polyhydric alcohol. When used alone, in liquid form, it serves as a glycerin substitute because it, too, has emollient and humectant properties. Fatty acids, when combined with sorbitol, yield nonionic surface-active agents. Sorbitan oleate, stearate, or laurate forms water-in-oil emulsions because it is dispersible in oil. If a polyoxyethylene group is added to these compounds, their hydrophilic properties are enhanced making them water dispersible. This, in turn, permits the formation of oil-in-water emulsions. Here again the dual action of surface-active agents is illustrated. The three hydroxyl groups in the sorbitol portion and the polyoxyethylene groups supply the hydrophilic action. The fatty acid portion of the molecule is responsible for the lipophilic activity. A trade-marked name for oil-soluble sorbitol derivatives is Spans* and for water-soluble sorbitol derivatives, Tweens.*

Another interesting group of nonionic emulsifiers includes the polyethylene glycol derivatives, which are marketed as Carbowaxes.† Most of them have a molecular weight of more than 1000. They are stable, water soluble and nonvolatile. Their density is directly proportional to their molecular weight. Thus Carbowax 4000 is harder

*Atlas Powder Co., Wilmington, Del.
†Carbide & Carbon Chemicals Co., New York, N. Y.

than Carbowax 1500. Therefore, polyethylene glycols, which vary from liquids to hard waxy solids, are well suited for use in unguent bases and lotions. They can be employed as wax substitutes to improve consistency or can be used in anhydrous bases to lend viscosity and body. Being water soluble, they do not interfere with washability of the unguent base. It should be noted that bases containing polyethylene glycols tend to become less viscous when too much water is added. This is due to the solubility in water of these glycols.

The washable unguent bases and lotions, which are the oil-in-water types, have many advantages over most others. They are easily removed from the epidermal surfaces by application of water or by simple wiping. This is of importance where removal from painful or sloughing areas is necessary.

Most emulsion bases and lotions are subject to some mold growth, making the addition of inhibitors necessary. Propyl and methyl para-aminobenzoate, known as the parabens, are best suited for this purpose.

The water content of the new unguent bases and lotions is protected by proper closure of the containers. A well-balanced formula should contain sufficient glycerin or other similar agents, which act as humectants and thus retard water evaporation. Being hygroscopic, they tend to attract moisture, thus maintaining an equilibrium between water loss and water gain.

When the new unguent bases and lotions are used alone, they serve as simple emollients and protective agents. However, the prime function of these preparations is to act as a vehicle or carrier for therapeutic substances prescribed by the physician.

Oil-in-water emulsions generally provide the means for epidermic action only. The degree of penetration into the skin of an unguent base or lotion or of medicinal agents is primarily determined by the physician and not by the pharmacist or chemist. He is best qualified to include the most desirable agents for individual treatment.

Lanolin, which increases the dermal penetration of an unguent or lotion, has been omitted from the formulae in this volume. The physician may include it if he chooses.

The anhydrous bases are hydrophilic. Some are designed to be very absorptive, while others are made to be primarily nonaqueous. These bases may be washable or nonwashable. Those able to take up large amounts of water are called absorption bases. The washable types consist largely of polyethylene glycols and/or methyl cellulose

mixtures. The nonwashable bases are composed mainly of petrolatum and a water-in-oil type of dispersing agent. These are absorptive and oilier than the washable bases.

Water-sensitive therapeutic agents, e.g., antibiotics, are reduced in potency or hydrolyzed in the presence of water. Therefore, anhydrous bases are used with these for effective therapy. The new anhydrous bases are also more pleasant to use than the older greasy, foul-smelling vehicles.

Homogenization, which reduces particle size and promotes dispersion, thus increasing emulsion stability, should be used whenever possible.

Unguent bases containing a very high percentage (over 50 percent) of water should not be used for water-insoluble drugs, such as salicylic acid, sulfur, and large amounts of oil. The formulae in this book were specially created to encompass as wide a range of application as possible.

TABLE 1

COMMON SURFACE-ACTIVE AGENTS

WATER SOLUBLE: PRODUCE O/W EMULSIONS

Type	*Example*	*Class*
Glyceryl Esters	Glyceryl Monostearate	Nonionic
Glycol Derivatives	Polyethylene Glycol Monostearate	Nonionic
Amine Derivatives	Triethanolamine	Nonionic
Polyoxyethylene Derivatives of Sorbitol Fatty Acid Esters	Tweens	Nonionic
Natural Gums	Acacia	Nonionic
Sulfated Fatty Acid Derivatives	Sodium Lauryl Sulfate	Anionic
Cellulose Derivatives	Methyl Cellulose	Nonionic
Soaps	Sodium Stearate	Anionic

OIL SOLUBLE: PRODUCE W/O EMULSIONS

Type	*Example*	*Class*
Lanolin Derivatives	Cholesterol and Oxycholesterol	Anionic
Sorbitol Fatty Acid Esters	Spans	Nonionic
Fatty Alcohols	Cetyl Alcohol	Nonionic
Metallic Salts	Sodium Borate (Borax)	Cationic

TABLE 2

COMMON INGREDIENTS OF UNGUENT BASES AND LOTIONS

WATER SOLUBLE		OIL SOLUBLE	
Name	*Function*	*Name*	*Function*
Glycerin	Emollient Humectant Texture aid Spreading aid	Cetyl Alcohol	Plasticizer Texture aid Absorption aid Emulsion aid
Propylene Glycol	Emollient Humectant Texture aid Spreading aid	Stearyl Alcohol	Plasticizer Texture aid Absorption aid Emulsion aid
Sorbitol	Emollient Humectant	Stearic Acid	Plasticizer Texture aid Absorption aid Emulsion aid
Polyethylene Glycols	Plasticizer Wax substitute	Beeswax	Plasticizer Emulsion aid Texture aid
Methyl Cellulose	Plasticizer	Petrolatum	Plasticizer Emulsion aid Drug carrier Texture aid Emollient
Water	Emulsion aid Solvent Washability aid Bulk donor Drug carrier	Liquid Petrolatum	Emulsion aid Emollient Texture aid Drug carrier
Methyl Paraben (Methyl Parabenzoate)	Mold inhibitor	Spermaceti	Plasticizer Texture aid Emulsion aid Absorption aid
Propyl Paraben (Propyl Parabenzoate)	Mold inhibitor	Cholesterol	Absorption aid Penetration aid
Glyceryl Monostearate	Plasticizer Emulsion aid Texture aid	Lanolin	Absorption aid Plasticizer Penetration aid

For some time, there have been conflicting reports regarding the efficient release of medication from unguent bases. There have also been mixed findings regarding the causes of drug inactivation. Some surface-active agents and several unguent-base compounds are said to neutralize the therapeutic action of drugs. There is insufficient

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