The Role of Fats and Fat Materials In Pharmaceutical and Cosmetic Preparations*

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FATS, fixed oils, and related materials have been used in the compounding of pharmaceutical and cosmetic preparations since the beginning of recorded history. The early literature and such records as the Bible abound in proof of this statement. Olive oil was probably the first oil known to Mediterranean civilization. Then, as other oils were recognized, the word oil acquired generic significance. These new oils became known as the oil of some plant or animal, e.g., oil of palm. In fact, for a time many substances which possessed the viscosity of oils, but were lacking in the other physical and chemical properties of such substances were also known as oils. This is the explanation of the term oil of vitriol for concentrated sulfuric acid. The ancients were not only familiar with fixed oils and their uses, but had some conception of the saponification of fixed oils with alkalies. Soap, according to Pliny, was first made by the Gauls from goat fat and beech ashes, and was applied to the hair to produce a blond or red effect. Later the Romans imported from Germany special soaps (probably with added plant dyes) for the same purpose. Many historians credit Galen (A.D. 131-201) as the first to mention soap as a detergent, but others claim that this property of soap was recorded some 450 years earlier. This, however, should be sufficient to convince one that the subject of fats and oils has long been one that has concerned the attention of man.

The present United States Pharmacopoeia and National Formulary set up standards for many members of this group of organic substances. When a substance is so described in one of these two books of standards it is termed an official substance. The official fixed oils are: Oleum Amygdalae Expressum U.S.P. (Expressed oil of almond), Oleum Chaulmoograe U.S.P. (Chaulmoogra oil), Oleum Gossypii Seminis U.S.P. (Oil of cottonseed), Oleum Lini U.S.P. (Linseed oil), Oleum Maydis U.S.P. (Corn oil), Oleum Morrhuae U.S.P. (Cod liver oil), Oleum Olivae U.S.P. (Olive oil), Oleum Ricini U.S.P. (Castor oil), Oleum Sesami N.F. (Sesame oil), and Oleum Tiglii N.F. (Croton oil). Individual fatty acids so recognized are: Acidum Oleicum U.S.P. (Oleic acid) and Acidum Stearicum U.S.P. (Stearic acid). Glycerinum, of course, is found in the U.S.P. The U.S.P. fats and waxes are: Adeps (Lard), Adeps Benzoinatus (Benzoinated lard), Adeps Lanae (Wool fat), Adeps Lanae Hydrosus (Hydrous wool fat or lanolin), Oleum Theobromatis (Cocoa butter), Sevum Praeparatum (Prepared suet), Cera Alba (White wax), Cera Flava (Yellow wax) and Cetaceum (Spermaceti). In addition, the official petroleum hydrocarbons which are used similarly to the fats, fixed oils and waxes must be enumerated. These are Petrolatum U.S.P. (Petroleum jelly or yellow vaseline), Petrolatum Album U.S.P. (White petroleum jelly or white vaseline), Petrolatum Liquidum U.S.P. (Liquid paraffin or mineral oil), and Paraffinum U.S.P. (Paraffin).

The question may now be asked: Why have the medical and pharmaceutical professions selected these fats and fat-like materials for official description? The answer most naturally is that these members of the fat group are the ones they most commonly use in medicine and in pharmaceutical and cosmetic preparations. Many members of this group may be used to protect surfaces against irritation. Since oils, fats and glycerin when applied to the skin tend to soften the epidermis they are termed emollients, and because of this fact are widely used in dermatological preparations. This corresponds to the natural mechanism for the protection of the skin surfaces, since the skin is normally covered with a thin layer of emollient oil. These oils and fats are for the most part inabsorbable by the cells; therefore, little or no direct effect can be produced on the cells. An adhesive coat is produced which prevents the irritation of drying, and the access of bacterial, chemical and mechanical irritants. This, then will explain the use of fats and fixed oils in lotions, sunburn preparations, liniments, antidotes for corrosive poisons, dressings for burns, etc. It is to be expected that, since these fatty products form adhesive coverings to the skin surfaces, they will often be used as vehicles (carrying agents) for the application of some other active medicinal agent to the skin. For example, olive oil in the medicated oils, wax and benzoinated lard in the cerates, waxes in the plasters, cottonseed oil in the liniments, cocoa butter in suppositories, glycerin in lotions, and wool fat, lard, spermaceti, wax and petrolatum in ointments.

When a medicinal agent is applied to the skin it may act locally (at the point of contact) or systemically after absorption from the skin. This brings up the age old discussion of the absorbability of an ointment base to enhance the absorption of the active medicinal agent. The petrolatums are said to be of value for superficial action only, while vegetable fats and oils are supposed to penetrate somewhat. However, many texts state that wool fat should be the base of choice when systemic action of a medicinal agent applied in the form of an ointment is desired. This statement is made on the basis of the similarity of the composition of wool fat to the natural skin fat, but it has never been proven to the satisfaction of many workers. In our laboratory it has been definitely shown that soaps made from individual fatty acids do irritate the skin to a different degree. If this can be taken as an indication of differences in penetration, then it is plausible that different fats made from single fatty acids might show a different skin absorbability. A certain mixture of such fats, synthetic or natural, might be proven to be the ideal ointment base where systemic action is desired.

When an active medicinal agent is applied to the skin in the form of an ointment, some consideration must also be given to the question of the distributive equilibrium of this agent in the ointment base and in the fluids of the skin. If the active agent is so soluble

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in the ointment base that the greater share always remains there, little action can be produced either locally or systemically. This is the explanation of the slight antiseptic action of phenol ointments, and the high percentage (5-10%) of phenol in carbolized oil used in the ear.

In addition to the facts enumerated it must be stated that when preparations are to be rubbed into the skin glands (inunction) the liquid or soft fats, such as the vegetable oils or lard, are the bases of choice. If protection and prolonged contact are desired, those properties are best secured by the harder and more adhesive agents, such as petrolatum mixtures and wool fat. True fats when rubbed into the skin gradually disappear, but mineral oils remain for a very long period of time and may eventually produce chronic irritation and fibrosis. If a fat or oil does not possess the proper consistency to be used alone, the common practice is to incorporate in preparations of those members with a low melting point certain quantities of the members with a high melting point. Thus the waxes are used to stiffen ointments. Paraffin may be used for the same purpose.

The fats and oils have the disadvantage of becoming rancid upon exposure to air, light and heat to give a product that is irritating and of a disagreeable odor. One method of eliminating rancidity is illustrated by the addition of benzoin to lard to give the so-called benzoinated lard. Another method is to dispense the ointment in air-tight containers. Wool Fat and the petrolatums, of course, do not become rancid. In both pharmaceutical and cosmetic preparations elegance is of some importance. Therefore, odor and color of these ointment bases receive considerable attention. Expense is another item of interest. Many feel that this is one reason why liquid petrolatum finds such a wide use in theatrical creams in place of fixed oils. Another point which must be emphasized is that lanolin differs from the other ointment bases in that it has the ability to mix without separation with about twice its weight of water. This permits the incorporation of aqueous preparations of medicinal agents.

When protectives are applied to mucous membranes they are termed demulcents. As a rule, they are viscid, water miscible solutions, such as the gums, since such substances adhere to moist surfaces better than do oils. Here again this corresponds to the natural protection of mucous membranes by mucus. In protecting mucous membranes demulcents reduce local chemical, mechanical or bacterial irritation much the same as emollients on skin, thus tending to diminish pain, reflexes, catarrh, spasms, etc. However, glycerin, a member of the group of drugs under discussion, is widely used as a demulcent as well as an emollient. The use of glycerin in cough remedies can be given as an example. Concentrated glycerin abstracts water from mucous membranes to cause a mild irritant effect. This is the explanation of the effectiveness of glycerin suppositories. Besides its uses as an emollient and demulcent, glycerin finds many uses in pharmacy as a solvent (second to water), sweetening agent, preservative, and as an agent to maintain the proper consistency of pill masses, extracts, etc.

We have discussed the emollient and demulcent use of the fat-oil group. Various members of this group have, in addition, internal uses. The true fats and oils have, of course, nutrient value; this is not true of the petroleum hydrocarbons. If excess quantities of fats and fixed oils are ingested the excess serves as an intestinal lubricant much the same as liquid petrolatum. Chaulmoogra oil has long been used to combat leprosy. It seems that everyone should be familiar with the use of cod liver oil as a source of vitamins A and D, and with the use of castor oil and croton oil as cathartics. The use of castor oil as a cathartic is interesting in that the oil itself is said to be nonactive. The active component is only produced upon saponification. Corn oil was introduced into the last pharmacopoeia because of its use in the preparation of the solution of Irradiated Ergosterol. The normal absorption of fats and fat-like materials from the gastro-intestinal tract and their subsequent use in the human body offers many scientific opportunities for future investigators. Already some evidence is available that certain fatty acids are essential to life and growth, but little is definitely known of the actual normal mechanisms of the absorption and metabolism of fats. Then too, clinicians know that in certain diseases, such as diabetes, the normal metabolism of fats is greatly disturbed. Some day definite knowledge of this subject may determine which fats and fixed oils are to be taken internally, as well as the form in which they are to be administered. In addition, it may control the fats in the diet during certain diseases. Little need be said of the incorporation of vitamins and hormones in cosmetics. The writer feels that it is largely the exploitation of a vitamin-hormone conscious public.

Of late, many new and nonofficial products related to fats and fixed oils have been found to be useful in pharmaceutical and cosmetic preparations. These included the so-called absorption bases which are unctuous fat-like masses containing cholesterol or oxycholesterol which permit the incorporation of varying amounts of water to produce a water-in-oil emulsion. In some commercial brands up to 50 per cent of a liquid, such as the Extract of Witchhazel, can be incorporated. Cetyl alcohol as well as stearyl alcohol produces the same type of emulsification. Glyceryl monostearate and sulfated and phosphated derivatives of cetyl and stearyl alcohol are being used in the preparation of creams. The sodium and triethanolamine salts of the alkyl sulfates are now to be found in shampoos, dental preparations, creams, liniments, ointments, etc. The wetting agents of the Aerosol type are likewise being used in shampoos, shaving creams, hand lotions, face creams, antiseptics, mouth washes, etc. Sulfonated olive and castor oils are being used extensively in shampoos and for the preparation of soluble oils and emulsions. The glycol derivatives of fatty acids are likewise finding their way into pharmaceutical and cosmetic preparations.

Pharmacists and the producers of cosmetics are agreed that these newer substances have a definite place in the manufacture of pharmaceutical and cosmetic preparations. They are more than satisfied with the finished articles so produced, but in many cases there still remains that big question: Are these newer agents free from all undesired physiological reactions? This question is forced by the new food, drug and cosmetic act, and it can be answered only by further pharmacological experimentation. Recently our own laboratory reported at the Atlanta Meeting of the American Pharmaceutical Association on the irritant action of the sodium salts of alky sulfates from C_8 to C_{18} inclusive on human skin. Of this series sodium lauryl and myristyl sulfates were the most active, but as a whole the alkyl sulfates were less irritant than ordinary sodium soaps. In further work dealing with the pharmacology of the fats, fixed oils and their related substances, the cooperation of the oil chemist is not only highly desired but is absolutely essential to success.

Natural and Synthetic Oils in Protective Coatings*

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Introduction:

The production and use of protective coatings stretches so far back into the past that its beginning antedates that of recorded history. There is left to us evidence of usage of such products even by prehistoric cave men. The coatings, then as now, were composed of two essential parts — pigment and binder or vehicle. That the pigments used then are still in use today can be proven. Determination of the nature of the medium used to bind the pigment is more difficult.

However, it can be determined from the records of earliest history that the use of oils of vegetable and animal origin has been known and practiced from the earliest times. Barring most recent progress the art of varnish making as practiced by the ancient Egyptians paralleled very closely in both method and composition of product that of the modern times.

Then, we may safely assume that for countless centuries drying oils have been an essential ingredient in the manufacture of protective coatings. The time of discovery of the two properties of the oils which have made them essential ingredients, viz., the ability to form hard tough dry films when exposed in thin layers to the air and also to become thickened when exposed to heat or sunlight, which thickened or polymerized oils produce smoother and more durable films of higher gloss, lies in the realm of conjecture.

That the property of certain oils to dry and polymerize constitutes the very foundation of the protective coatings industry today is beyond argument. Certainly, the nature and mechanism of these two phenomena known for so long and constituting as they do the corner stone of a vast industry must be very thoroughly understood.

Unfortunately, such is not the case. In spite of the work of numerous investigators, no entirely satisfactory explanation for the mechanism of oil drying or polymerization has yet been advanced. A vast store of empirical information has been accumulated by the protective coatings producer, but fundamental explanations have yet to be made. That considerable progress has been made cannot be denied and practical use has been made of hypotheses advanced. Solution of the fundamental problem will constitute a major step forward, but that step lies in the future. A brief review of some explanations for the phenomena may be of interest.

Drying and Polymerization of Oils:

The ability of an oil to dry is associated with unsaturation of the molecule — measurable by means of the iodine number. Iodine number is not a true measure of drying, but is rather approximate. However, as a general rule, the higher the iodine number, the better drying qualities an oil has.

The drying of an oil appears to involve two types of reactions best described as double bond polymerization and absorption of oxygen. Absorption of oxygen has long been regarded as essential in oil drying. Recently, the theory of "gas coagulation" has been advanced by Auer, but has not received widespread support. The nature of double bond polymerization has been discussed by Cutter and Jordan as a modification of the Diels-Alder reaction, which serves to give a six membered carbon ring linking together two acid radicals of the triglyceride.

Long neglects double bond polymerization entirely and concludes that drying takes place in two stages. The first, the absorption of oxygen to form polar molecules, and second, the association of liquid polar molecules to form a solid insoluble phase. Since we have no means of following molecular weight change beyond the point at which insoluble products are produced, our knowledge of the nature of the insoluble phase is limited.

When a drying oil is polymerized by means of heat, the changes taking place in physical properties are well known. The oil increases in specific gravity and viscosity. The iodine number drops and the acid number rises. The color of the oil becomes darker and there is an increase in molecular weight. The chemical reactions accompanying these physical changes are unexplained. Work in the synthetic resin field has raised some interesting parallels. Once more the diene reaction is thought to play a vital part.

The Drying Oils:

Moving from a field in which speculation plays such a large part onto firmer ground, the constitution of the drying oils is well established. Natural oils which possess the ability to dry are the triglycerides of fatty acids mainly of the linoleic or linolenic series. The natural oils never contain a single fatty acid, but invariably a mixture of acids of varying degrees of unsaturation. That presence of saturated acids in large quantity will reduce the ability of an oil to dry and that presence of a highly unsaturated acid in large quantity will increase its drying power is generally conceded. The individual drying oils of large usage in protective coatings manufacture and their main usage are as follows:

Linseed Oil:

Predominating fatty acids going to make up the ester that is linseed oil are linoleic acid carrying two double bonds and linolenic carrying three double bonds. Approximate percentages are 60% linoleic and 25% linolenic. The remainder is stearic, palmitic, and oleic, all non-drying acids.

Linseed oil is an excellent drying oil and was long the paramount oil for both paint and varnish. It still

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