

Do not use medical terms when discussing products with the physician; use pharmaceutical terms.

Do not yourself, or permit your assistants to conduct themselves in any such manner so that professional atmosphere will be destroyed, or reflect on the professional integrity of the store.

In conclusion may I state that each of these practices has been found practical in its application and am confident can readily be applied in any professional pharmacy whose practices should whole-heartedly and sincerely engross a professional atmosphere. The professional pharmacy of to-day has a great responsibility in the program of public health service. With the endorsement of the medical profession, patronage of the public and recognition by the pharmaceutical societies, this type of pharmacy will become more and more recognized as a preferable outlet of pharmaceutical service.

CALCIUM LINOLENATE.*

BY KATHRYN GLENNON.¹

Since the work of G. O. and M. M. Burr, at the University of Minnesota, which clearly discloses that some fats contain indispensable unsaturated fatty acids called Vitamin F, and that linseed oil and lard are characterized by varying yet large amounts of the Vitamin F ingredient, it seemed possible that an entirely new concept could be reached in a better understanding of the pharmacologic action of official lard and official linseed oil used as bases in ointment, liniment and the like.

It will be recalled that they conclusively demonstrated that animals reared on diets free from indispensable unsaturated fatty acids developed typical lesions of the skin which amounted to a dryness and roughness eventuating in eczema; and that the hair and nails similarly suffered dryness, roughness, brittleness and other changes suggesting atrophic disorders. Also, it will be recalled that the administration of exceedingly small amounts of indispensable unsaturated fatty acids, or Vitamin F, could either prevent or cure the lesions in rats subjected to this type of diet.

Lard has been an official ointment base for many years, and a review of the dermatologic literature reveals that much of the standard medication used in the external treatment of certain eczemas has remained the same for the past fifteen or twenty years, excepting that the base, generally lard, has been displaced with petrolatum or one of its many equivalents. Similarly, it would appear that the report of two decades ago clearly suggested far more favorable response to the earlier ointments than is now recorded for the present-day ointment; and since the medication has remained the same, it would seem, in the light of the discovery of the Burrs, that the lessened efficiency of the treatment might probably be ascribed to the change in the ointment base.

With these considerations in mind Dr. Weinstein and I prepared an ointment which had for its principle the blending of the natural lipids of the skin in-

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cluding lecithin and cholesterol in a base of lard, reënforced with Vitamin F or unsaturated fatty acids. The clinical effectiveness of this ointment has been separately reported and amounts to a complete corroboration of the work of the Burrs with respect to the human. In other words, many conditions which the Burrs have found to be the result of Vitamin F deficiency in the experimental animal and which seemingly have a counterpart in the human have responded to the topical application of an ointment compounded essentially of the skin lipids with accentuated reënforcement of the Vitamin F ingredient.

It will be observed that topical application was effective in these human cases, thus disposing of the question as to whether or not externally applied vitamin preparations can be effective. It can now be said with complete clinical assurance that conditions resembling Vitamin F deficiency may yield to the external application of Vitamin F applied to the skin in the form of a suitable ointment. This is not an indication that all vitamins applied externally will be effective, since all vitamins have comparatively minor parts to play in skin function. But the withdrawal of Vitamin F from the diet of the animal produces typical skin lesions of an eczematous nature which unquestionably yield to the external application of highly enriched Vitamin F ointments. In this sense Vitamin F certainly is deserving of the designation "the skin vitamin," in the same sense that Vitamin D is called "the sunshine vitamin."

Whereas the effectiveness of Vitamin F ointment locally applied is seemingly unquestionable, from the standpoint of the pharmacist there is a compounding difficulty that requires study and correction. Lard, as is commonly well known, is subject to rancidity. The addition of unsaturated fatty acids to lard may in a number of instances foster this rancidity. A rancid ointment does not always result from the incorporation of Vitamin F in lard, but when it does, the ointment may become an actual irritant particularly if used on the tender skin of the infant.

The use of oils, such as linseed oil, for the purpose of securing Vitamin F in its natural state is considerably limited by the fact that in order to obtain sufficient concentration of Vitamin F in the ointment it is frequently necessary to exceed 60% or 70% level in the form of oil; and ointments containing 60% to 70% of oil are naturally fluid and unsuitable for common use by reason of their undesirable consistency; hence, the desirability of procuring Vitamin F in concentrated form.

Many esters of Vitamin F have been prepared, as for example the methyl ester, the ethyl ester and others. Not all of these esters are equally effective, and some can be considerably dangerous. It is commonly well known that the methyl derivative of many products, such as methyl alcohol, are quite toxic. They are unsafe for extended clinical use and should not be selected if they can be replaced by non-toxic effective compounds.

The esters of the fatty acids have been ushered into use largely by reason of the belief that their form permitted absorption as suggested by their solubility. However, a common experience indicated that perhaps the calcium salt of the linseed oil fatty acids could also be quite effective particularly in the treatment of first and second degree burns. Obviously, this indication is implied by the effectiveness of Carron Oil, or Lime Liniment, which is a mixture of linseed oil and lime water and produces a calcium soap which partially emulsifies the oil. Certainly, the water and the oily glycerides are nothing to commend in the treatment of burns;

and if there is any specific effectiveness in the use of Carron Oil, it seems possible that it might be linked with the calcium salt of the Vitamin F component of the oil.

It is not difficult to prepare the calcium salt of the effective unsaturates. The exact identity of the unsaturated fatty acids responsible for the Vitamin F effect is not known. It is merely assumed that they belong to the linoleic, or to the linolenic, or probably to both groups of unsaturated fatty acids. It may be an isomer of either linoleic or linolenic or it may be one of the isomeric form of either linoleic or linolenic acids. Thus, the common statement that because linoleic acid is probably widespread in natural foods and, therefore, a Vitamin F deficiency is not likely to exist, is completely indefensible on the ground of scientific data. Since the exact nature of Vitamin F is not known, and the exact distribution of that particular compound is also unknown, such statements are entirely unwarranted and are calculated simply to mislead rather than to clarify the topic under investigation. However, for purposes of brevity, we shall designate the calcium salts that are known biologically to be effective under the generic title of Calcium Linolenate, it being understood that by calcium linolenate we are not referring to a specific chemical compound but to a mixture representing the calcium salt of the indispensable unsaturated fatty acid—or the calcium salt of Vitamin F.

The neutralization of Vitamin F unsaturates prepared properly from linseed oil with calcium hydroxide is all that is required for the manufacture of the product. The product can be purified further by frequent washings with ethyl alcohol to remove all of the free acids that have not combined with the calcium. Obviously the product is not a single chemical compound but it results in a whitish powder, insoluble in water, readily incorporated in fat and fat-like material and, most important of all, it is seemingly as effective as are the unsaturated fatty acids from which the calcium salt is derived. This implies that calcium apparently seems to select the more active fatty acids, because, if this were not true, then the calcium salt should only be about half as effective as the unsaturates from which it is prepared. Since it is of equal effectiveness, it suggests that about half of the unsaturates in a mixture of such acids are effective and that the calcium combines with that particular half.

In addition to its effectiveness which is seemingly identical with the effectiveness of the unsaturates from which it is derived, calcium linolenate is apparently stable under a great variety of conditions which makes it ideally suited for incorporation in ointments, cerates, unguents, oils, creams and similar preparations for external application. The dosage level of calcium linolenate is not entirely known but seems to be effective at about from 5% to 10%. If lard is used as the base to which calcium linolenate is added, rancidity is not particularly fostered as is the case when the unsaturated fatty acids themselves are used. However, an outstanding quality of linolenate is the ability to dispense with lard and to replace lard with petrolatum. It is true that petrolatum probably does not permit of the same degree of intradermal penetration as does lard and certain other fats; but this intradermal penetration can be conferred upon petrolatum through the simultaneous addition of lanolin and lecithin. Accordingly, a suitable Vitamin F base, without rancidity, with good absorption and with the specific effect of preventing and correcting the skin disorders that arise in consequence of Vitamin F deficiency can be

compounded through the use of calcium linolenate according to a formula patterned somewhat as follows:

Calcium Linolenate.....	5.0
Lecithin	5.0
Anhydrous Lanolin.....	5.0
Petrolatum, white or yellow.....	85.0

An ointment compounded on this basis needs no additional medication for the correction and prevention specifically of allergic eczema—the type which apparently develops because of Vitamin F deficiency.

Not only is the ointment suggested suitable for the treatment of specific eczemas, but it lends itself admirably well for the treatment of first and second degree burns. It is, in reality, a Carron Oil in solidified form or, more properly, it is the active ingredient of Carron Oil in a proper pharmaceutic ointment base.

Calcium linolenate ointment has been used on a few occasions to displace petrolatum in the treatment of osteomyelitis, and although the reports are few, they are unanimously highly satisfactory. It appears that packings of calcium linolenate ointment as formulated above not only served the purpose of petrolatum, which comprises 85% of the ointment, but displays at the same time a bacteriostatic effect and a definite bone proliferative effect. It is well known that the unsaturated fatty acids are quite selective in their ability to destroy and inhibit the activities of certain bacteria. Apparently, calcium linolenate slowly releases the Vitamin F and makes for a long-continued activity of this slow bacteriostatic effect which is probably helpful in the treatment of osteomyelitis.

An unusual and interesting use for calcium linolenate is its incorporation in talc intended for use on the baby. From 1% to 3% of calcium linolenate mixed with talcum and perfume and intimately ground in through the use of the ball mill produces a medicated talc which seems to act with unusually splendid effect in overcoming the rashes to which the baby is subject with far greater promptness than talcum not so medicated.

A most effective use of calcium linolenate ointment is in the prevention, and better, in the treatment of erythema solaris or sunburn.

While we are not prepared to discuss the biologic activity of calcium linolenate as standardized by assay, we are sufficiently advanced in our study to suggest that calcium linolenate is most effective when prepared from unsaturates whose biologic assay in Shepherd-Linn units has been established. In other words, if the biologic activity of the unsaturates is known, the biologic activity of the calcium linolenate can be quite accurately expressed.

Calcium linolenate is a tremendously effective protective ingredient and seems to have every possibility of displacing zinc oxide. Since it is needed in only one-tenth the amount that is required of zinc oxide, a 1% calcium linolenate ointment being fully as protective as a 10% zinc oxide ointment, it follows that such ointments are much more economical for general hospital use since the unit cost of calcium linolenate is considerably less than ten times that of zinc oxide.

BIBLIOGRAPHY.

(1) Burr, G. O., and Burr, M. M., "On the Nature and Rôle of the Fatty Acids Essential in Nutrition," *J. Biol. Chem.*, 86, 587-621 (1930).

- (2) Cornbleet, T., "Use of Maize Oil (Unsaturated Fatty Acids in the Treatment of Eczema)," *Arch. Derm. and Syphil.*, 31, 224-226 (1931).
- (3) Burr, G. O., Burr, M. M., and Miller, E. S., "On the Fatty Acids Essential in Nutrition," *J. Biol. Chem.*, 97, 1-9 (1932).
- (4) Evans, H. M., and Lepkovsky, S., "Vital Need of the Blood for Certain Unsaturated Fatty Acids," *J. Biol. Chem.*, 99, 231-234 (1932).
- (5) Hansen, Arild E., "Study of Iodine Number of Serum Fatty Acids in Infantile Eczema," *Proc. Soc. Exper. Biol. Med.*, 30, 1198-1199 (1933).
- (6) Hansen, A. E., "Serum Lipid Changes and Therapeutic Effects of Various Oils in Infantile Eczema," *Ibid.*, 31, 160-161 (1933).
- (7) Oncken, Mildred, "Unsaturated Fatty Acids (Vitamin F) Deficiency," *Ill. Med. Jour.*, 67, 236-239 (1935).
- (8) Shepherd, M. I., "Vitamin F in Skin Creams," *Drug and Cosmetic Ind.*, 12, 30 (1936).
- (9) Glennon, Kathryn, "Vitamin Soaps," *Soap*, (November 1936).
- (10) Weinstein, M. L., and Glennon, Kathryn, "Vitamin F Ointments," *Ill. Med. Jour.*, (June 1937).

COMMENTS OF AN EXPERIENCED HOSPITAL PHARMACIST.*

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So much has been said recently relative to the establishment, standardization and conducting of a hospital pharmacy that it would seem there is little left to be commented upon. However, to make a story more impressive it needs to be repeated over and over again. Each reading makes a new and different impression on the mind, thus helping one to obtain more useful knowledge than might be gained from a casual reading. If, in the short space allotted to this paper I may make some suggestion or even repeat some thought oft expressed, which will be of some value to a fellow member, I shall feel well repaid for my humble effort.

First we might ask what is a hospital pharmacist? The most natural answer to this question would be "one who dispenses drugs in a hospital." However, if we stop to look over the field we come to the conclusion that hospital pharmacists at present may be nurses, doctors, internes or even (though I blush to mention it) sometimes maids and janitors. It is my humble opinion that a hospital, however small, should be placed under the same restrictions, regarding the dispensing of drugs, as any drug store, and required to have a registered pharmacist in charge at all times.

The dispensing of drugs to patients in hospitals is, to my mind, an important professional duty and should be entrusted only to one who has been educated and trained for that particular purpose. The professional duties are far more complicated and extended than those of an ordinary pharmacist and I am heartily in accord with the idea of pharmaceutical internship as is being formulated by some of our more prominent Schools of Pharmacy over the country.

The practicability or feasibility of such an internship has been forcibly brought to the writer's attention on many occasions when after employing an assistant pharmacist who had come with the best of credentials as to character, education, ability and ambition, it became necessary to spend much time and patience in ac-

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