

CLINICAL INVESTIGATION OF BENTONITE-PETROLATUM OINTMENTS AND OINTMENT BASES*

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Since September, 1943 we have conducted extensive clinical investigations at the Pittsburgh Skin and Cancer Foundation with pastes and ointment bases containing petrolatum and bentonite developed by the multiple fellowship on petrolatum at Mellon Institute.

These pastes and ointment bases have all been of the washable, oil-in-water emulsion type, and of considerable hydrophilic capability, owing to their bentonite content. Because of the presence of this colloid, the bases are physically stable, even if subjected to high temperatures or freezing conditions. Thus they may be sterilized by autoclaving, if the need exists for it, without causing them to melt or break down in any way. The experience gained with these pastes and ointment bases and a summary of the clinical findings are reported in this paper.

NOTES ON THE PHARMACOLOGY OF BENTONITE

The properties and uses of bentonite have been reviewed by Davis *et al.* (1) and by Lesser (2). They have described it as a claylike substance derived from volcanic ash, characterized by unique *gelation* and swelling properties attributable to its strong affinity for water.

Although bentonite has been employed in medicine both internally and externally, it is chiefly recommended as an ingredient of preparations for dermatologic use. Its colloidal nature confers detergent properties and the ability to absorb moisture and obnoxious debris from the surfaces of the body. Bentonite possesses salt-forming properties. In common with other hydrous aluminum silicates it forms stable salts with organic bases, including alkaloids and proteins. In an acid environment it removes proteins from water solution or suspension, as insoluble salts. This property undoubtedly extends to the fixation of proteins in serous exudates.

The inherent beneficial action of this colloidal substance may be enhanced by the addition of therapeutically active substances to well-composed bentonite-based preparations, for they possess excellent suspending and dispersing properties and present few problems related to pharmaceutical incompatibilities. If they are properly formulated and compounded, preparations made with bentonite are suitably protective and tenaciously adherent; and because of their strongly hydrophilic nature, they can be washed readily from the skin without going through the messy procedure of cleansing with oil, so frequently necessary with ointments and pastes of the non-hydrophilic variety. Thus these preparations should be more acceptable to the dermatologist and the patient alike than are greasy ointments and pastes.

The official use of bentonite in the U.S.P. XIII is in Bentonite Magma, which

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contains 5 per cent of the material dispersed in water. This magma is employed as a suspending medium in Chalk Mixture (used internally) and in Calamine Lotion; it is also employed in the Neocalamine Lotion of N.F. VIII.

Brown (3) described the use of bentonite as a vehicle for medicinal and cosmetic pastes. Kellogg (4) has advocated its use as a hand-protecting cream against oils and greases in the following formula: bentonite 17, soap 4.5, water 78.5. Haraldson (5) has employed bentonite as a base to carry formalin as a fungicidal agent. Griffon (6) used it in the preparation of an ointment base. Jung (7) described its properties and the manner of its application as a therapeutic agent.

Tainter *et al.* (8) described bentonite under the name of Elkonite as a colloidal clay composed chiefly of aluminum magnesium silicate, which is hydrophilic and which swells in water to form a gel in 15 per cent concentration. They stated that the addition of acid or alkali to fluid suspensions increases the hydrophilic property as demonstrated by increases in viscosity. They also spoke highly of the absorptive quality of this colloid. Further, they mentioned that the most promising use for clinical purposes appeared to be as an ointment base consisting of a 15 per cent gel.

Our experience, however, indicates that where an unmodified bentonite gel is used as ointment base, it is likely to be unsatisfactory. If a layer of bentonite gel is applied to the skin and allowed to dry, it forms a hard crust which contracts and cracks as drying proceeds. The shrinkage produces an uncomfortable pulling sensation, and the dry, cracked crust brings about mechanical irritation which causes a friction-dermatitis. Therefore, we do not advise the use of a bentonite gel alone as an ointment base under circumstances where complete drying of the ointment can occur. This objection has also been raised in a recent publication by Hopkins (9), who recommended the use of a number of additives to overcome the difficulty. He used these bases in over 500 cases without finding evidence of irritation or sensitization. He stated that the gels are suitable carriers for sodium penicillin or any water soluble drug and also for sulfonamides, fatty acids, salicylic acid and other treatment agents which may be dissolved in propylene glycol, alcohol or other suitable solvent before being added to the prepared base. Sulfur, ammoniated mercury, zinc oxide and other insoluble powders were said to be readily incorporated in these bases.

Hopkins pointed out that bentonite gels should not be used in wounds because of the insoluble material so introduced. He also found them to be unsatisfactory in intertrigo of the toes or elsewhere, because if applied thickly, they sometimes form hard sharp granules as they dry out. However, the particular bentonite formulations which we have investigated have been used successfully in this manner in a number of individuals. In one chronic case of a dermatophytosis involving the toes, these preparations combined with various fungistatic agents have been used almost daily for the past four years, first for treatment and then as a preventive measure, with no evidence of irritation appearing at any time.

Kulchar (10) advocated the use of 15 per cent suspensions of bentonite for eruptions and also for essential pruritus of the anogenital region. Soldi and

Cuccia (11) described a paste made of bentonite, water and glycerin; they used it as a substitute for fat or petrolatum as a base for ointments. Cox and Goedrich (12) furnished a formula for a "Soluble Ointment Base"; this consisted of glyceryl monostearate, glycerin, bentonite, and water. Maney and Jones (13) stated that bentonite acts as a binder and can be used to prevent separation of the ingredients of compound ointments; two per cent of the clay was added to the mixture. Knowles *et al.* (14) credit Osborne with calling attention to the value of bentonite in 3 per cent and 6 per cent aqueous suspension as a dermatologic topical liniment. Goodman (15) has described the use of bentonite as a major ingredient in a number of formulas intended for application to the skin or scalp. We have found, however, that the directions accompanying many of these formulas are not adequate for the preparation of products of pharmaceutical elegance and suitable for topical medication.

DESCRIPTION OF THE HYDROPHILIC OINTMENT BASES USED IN THIS STUDY

The ointment bases embraced in this study consist essentially of emulsified petroleum jelly, the emulsifier being hydrated bentonite. The physical properties of the emulsion are modified by the addition of small amounts of other well-known emollients. The use of preservatives is essential, and several official products are satisfactory. The oil phase content of the formulations has ranged from 10 to 32 per cent, and satisfactory emulsions have been obtained with bentonite concentrations of 13 to 17 per cent. A typical formula employed is as follows:

Petrolatum.....	32.0%
Bentonite.....	13.0
Methylparaben.....	0.1
Sodium Lauryl Sulfate.....	0.5
Water.....	54.4
	<hr/> 100.0

Preparations containing low levels of petrolatum are satisfactory as the rub-in type of ointment base which can be thoroughly dispersed on the skin like a vanishing cream, but a considerably higher oil phase content was found to be necessary whenever ointments were to be applied in thick layers. By thus increasing the emollient qualities of the bases, drying effects and the possibility of producing mechanical irritation of the skin were eliminated without impairing the water-removability and other desirable properties of the ointments. These high oil-content formulations are compatible with a wide variety of drugs, and they have been employed successfully in the present study as the bases for several ointments, as outlined in succeeding sections. Extensive clinical use has also shown that they possess definite therapeutic properties without the addition of any "active" medicament.

SKIN SENSITIVITY TEST

The initial question was whether emulsion bases of this type would cause any skin irritation because of their inherent chemical properties or because of any

latent allergenic qualities. Two hundred individuals, most of whom had some form of dermatitis, were patch-tested with one of these ointment bases. These patch tests were permitted to remain in position for a period of one week. At the end of this time, the patches were removed and any reactions due to a primary irritant effect of the ointment were noted and the sites of the patch tests were then marked with indelible ink. The subjects were asked to return one week later, when a second patch test was applied directly to the previously marked area and again these patches were permitted to remain in place for one week. At the end of this time the patches were removed and any reactions attributable to sensitization by the first tests were noted. The results of this patch-testing established the fact that this preparation was relatively safe for use. Only one subject in the group of 200 was found to have a small area of irritation or dermatitis at the end of the first patch-testing period, which established the fact that, in the group of individuals who were tested, this preparation was essentially not a primary irritant. A dermatitis designated as ++ was noted on the same subject at the end of the second patch-testing period. This was interpreted as a reaction of sensitization. This preparation therefore acted as a sensitizing agent in only 1/2 of 1 per cent of the 200 individuals tested. In view of our previous experience with ointments of all types, we consider this amount of irritation to be unusually low.

OINTMENT BASE CONTAINING BORIC ACID

We added 5 per cent of boric acid to a petrolatum-bentonite gel emulsion base containing 32 per cent of oil phase and applied it in the treatment of numerous skin diseases. (While this experimental and clinical work was in progress we became increasingly aware of some of the unsatisfactory effects attributable to boric acid. Therefore, after the preliminary therapeutic testing reported in this chapter had been completed, we investigated the same ointment base without the addition of boric acid and found that the results in almost every instance were equally, if not more, satisfactory.) Although the ointment base with boric acid was used in the treatment of a great number of individuals, a complete record of observations was made for only the first 157 patients. In some instances the preparation was of primary therapeutic importance, while in others it was used as an auxiliary treatment.

The ointment base containing boric acid was applied in 34 cases of eczema of the leg. Good results were obtained in 30; no improvement occurred in 4 instances—an unusually high proportion of good results. The non-irritating character and high absorptive ability of this preparation proved to be of great therapeutic value. Ordinarily the ointment was applied in a thick layer, which was covered with gauze, fixed with a loose circular bandage and kept in place for a period of one week. Comparative tests were made using the ordinary Lassar's paste (Zinc Oxide Paste, N.F.). In most instances the special ointment base with boric acid was found to be superior. At the time for redressing we found that the hydrophilic type ointment was more easily removed, that the skin was softer and more pliable and that the inflamed area was made ready for

reapplication with less effort and less discomfort than when the Lassar's paste was used.

Twenty-three patients having dermatitis of the hands caused by soap and water were treated. These included vesiculo-erythematous, dorsal nummular, deeply fissured thick palmar, and the fine blistery interdigital varieties. Dressings were fixed in place with bandage twice a week. The use of soap and water was stopped, and 38 r of superficial X-ray was given once a week. Good results were obtained in 16 patients; in 7 patients the results were indifferent or bad.



FIG. 1. SHOWING AN INDOLENT LEG ULCER AND VESICULO DERMATITIS SURROUNDING IT

In 22 patients suffering from leg ulcers of varied etiology this ointment was used in an auxiliary capacity in the following manner: the skin surrounding the leg ulcer was covered with a thick layer of the ointment, while the bed of the ulcer was coated with sterile sulfanilamide crystals. The object of this procedure was (a) to protect the skin from the irritating discharges of the ulcer; (b) to protect it also from the likelihood of becoming sensitized to the sulfanilamide. In 19 patients the results were satisfactory; in 3, the treatment had to be discontinued, because of adverse effects.

Sixteen patients were treated with the ointment during the final stages of infectious eczematoid dermatitis, that is after vesiculation and pustule formation had been effectively controlled, and where the therapeutic need consisted of softening the dried and fissured skin; the treatment was satisfactory in 11 and unsatisfactory in 5 patients. It must be noted especially however, that some of the most satisfactory results from the use of this preparation occurred in this group of individuals who are so notoriously ointment- and drug-sensitive.



FIG. 2. APPEARANCE OF LEG 4 WEEKS LATER

Of 9 patients presenting neurodermatitis, the ointment was satisfactory in 7, unsatisfactory in 2.

Of 8 patients presenting pyoderma, it was satisfactory in 5, unsatisfactory in 3.

In 6 patients suffering from extensive psoriasis of the legs this ointment was used in combination with autohemotherapy and liver injection. It worked well in 5 instances.

In 7 patients presenting fixed dermatitis medicamentosa caused by one of the sulfonamides, satisfactory results were obtained in 6 instances.

Of 6 patients with atopic dermatitis, in 2 the results were as satisfactory as with any other ointment used, while in 4 the applications had to be discontinued.

Of 4 patients presenting dermatitis of the fingertips, good results were obtained in 3. The dermatitis of the fourth patient was found to be caused by the application of Tincture Merthiolate; when this was stopped, the dermatitis disappeared.

Six patients presenting dry, scaly, circinate dermatophytids responded well to the ointment, which, of course, was supplementary to the treatment of the primary dermatophytosis.

In 3 instances of acrodermatitis chronica atrophicans the results were good.

TABLE I

Summary of clinical findings with ointment containing 5 per cent boric acid in petrolatum-bentonite emulsion base

	GOOD	INDIFFERENT	UNSATISFACTORY*	TOTAL
Leg eczema.....	30	4		34
Soap and water dermatitis of hands..	16	4	3	23
Leg ulcers.....	19		3	22
Infectious eczematoid dermatitis.....	11		5	16
Neurodermatitis.....	7	2		9
Pyoderma.....	5	3		8
Psoriasis of legs.....	5	1		6
Dermatitis medicamentosa (sulfonamides).....	6		1	7
Atopic dermatitis.....	2		4	6
Dermatitis of fingertips.....	3	1		4
Dermatophytids.....	6			6
Acrodermatitis chronica atrophicans..	3			3
Miscellaneous.....	10	3		13
Total.....	123	18	16	157

* The term "unsatisfactory" signifies that a dermatitis occurred, but in no case was it more severe than that produced in the same patient by other topical medication.

In 13 patients presenting dermatitis of variable cause, including cosmetic dermatitis, good results were obtained in 10, and no improvement occurred in 3.

Thus in a total of 157 patients treated with the ointment base containing boric acid, good results were obtained in 123 (78.3 per cent), while 18 patients (11.5 per cent) were not benefited and 16 (10.2 per cent) were adversely affected (Table I).

MERBROMIN N.F. AND SALICYLIC ACID OINTMENT

For the treatment of atopic dermatitis with secondary infection, an ointment was prepared containing 1.5 per cent salicylic acid, 2.0 per cent merbromin, and 96.5 per cent bentonite-petrolatum ointment base with high oil content. In 8 patients with atopic dermatitis affecting the ears, neck, nape of neck, face, scalp, and popliteal areas, this preparation was found to be of value in 3 patients

and of no value in 4 individuals. One patient was irritated by the preparation after keeping it on for 24 hours. The method of application of this preparation was to spread it lightly over the affected areas, cover it with a piece of gauze and keep it in place by a light bandage. The paste was permitted to stay in place for 24 hours and was then removed. Any accumulation of this preparation was easily washed off with tepid water.

OINTMENT OF COMPOUND TINCTURE OF BENZOIN

For dermatitis which occurred in senile atrophic skins, an ointment was prepared containing 1 per cent of Compound Tincture of Benzoin in this emulsion type base. This preparation was used on patients who presented a fine erythematous squamous acrodermatitis and it was found to be quite satisfactory.

UNMEDICATED OINTMENT BASE

The satisfactory results obtained in the 123 of the first group of 157 patients treated with the bentonite-petrolatum emulsion containing boric acid prompted us to use this preparation in a routine fashion for over two years. During this period we learned that when the ointment was stored for several months, various sized crystals of boric acid would develop throughout its mass, thus handicapping its usefulness. We also became aware of the reported toxic effects of boric acid when it happens to become absorbed. These circumstances induced us to try the bentonite-petrolatum emulsion base without the addition of boric acid. Our results were so satisfactory that since then we have continued to use the unmedicated ointment base in all types of cases except those classified as dermatitis caused by soap and water, where we found that the boric acid ointment gave superior results. Since the pH of the base itself is about 7.5 and that of the base containing the boric acid is 5.5 it occurred to us that the slight acidity of the latter was responsible for its greater value. We have investigated this possibility, using an unmedicated ointment base adjusted to a pH of about 6.0 with a citrate-phosphate buffer system. Observations in more than 100 patients bear out the above belief since the latter base acts as efficiently as the ointment base containing boric acid in the treatment of the dermatitis caused or aggravated by soap and water.

We have also found that the petrolatum content of the base can be reduced to 25 per cent without impairing its emollient properties, a quality most desirable. This latter preparation has advantages from a pharmaceutical standpoint, since it is easier to compound, and also it makes a better stock base for the preparation of ointments.¹

SUMMARY AND CONCLUSIONS

A 4-year study has been made of a type of hydrophilic ointment base which consists essentially of petrolatum emulsified in a bentonite gel. There are the

¹ We wish to thank Baybank Pharmaceuticals, Inc., Division of Chesebrough Manufacturing Company, Cons'd., New York, for their liberal contribution of "Terakon" Ointment Base, which is essentially of this composition.

following advantages to be gained by adding a preparation of this kind to the list of dermatologic topical applications:

1. A new absorbing paste or ointment base is made available.
2. The preparation exhibits valuable therapeutic properties.
3. It is compatible, both pharmaceutically and therapeutically, with a wide variety of useful drugs.
4. The ointment base is composed of relatively non-irritating substances, and allergic skin reactions to it are rare. (When patch tests were performed on 200 patients, only 1 individual, who was suffering from an atopic dermatitis, showed a slight skin sensitivity to it.)
5. We, as others, have observed that the use of topical applications for treating chronic dermatoses over an extended period may result in a decrease or complete loss of their therapeutic efficacy. In such cases it is advantageous to resort to an entirely different type of preparation, and the bentonite-petrolatum ointment base is suggested.
6. It is an alternative preparation for use instead of Lassar's type of paste.
7. By far the largest group of patients treated with this preparation during the 4-year study had skin diseases of the lower extremities. These disturbances included hemostatic dermatitis, varicose dermatitis, dermatitis medicamentosa, dermatitis which was the result of atrophy, and the dermatitis which came from bath itch, dermatophytids and infectious eczematoid dermatitis. Except in certain instances noted in this report, the bentonite-petrolatum ointment base was not only well tolerated, it was highly beneficial.
8. The ointment base is of value as a protective cup in treating leg ulcers, as is also described.
9. In the vast majority of instances of soap and water dermatitis, which is one of the more recalcitrant types of dermatoses, the effect of a bentonite-petrolatum ointment base containing boric acid is excellent, and it rapidly ameliorates the subjective symptoms of burning and itching. Equally satisfactory results are obtained without the use of boric acid if the ointment base is adjusted to a pH of about 6 with a citrate-phosphate buffer system.
10. The special colloidal properties of bentonite make the ointment base of great value as a medium for absorbing moisture and obnoxious debris from the surface of the skin.
11. The preparation can be removed from inflamed areas without the use of liquid petrolatum or other oils, a procedure which is messy, lengthy and unpleasant; washing with a small quantity of water is ordinarily sufficient, and except in the most unusual cases, this cleansing procedure does not increase the irritation or inflammation of the skin.

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