may be added directly to a water suspension of finely divided pectic acid or to a water solution of the pectinic acid. In other cases where the organic reagent is not water soluble, it may be used in the form of a solution in a suitable organic solvent. Care must be taken not to have present any great excess of the base. Preferably, the total amount of base added should be slightly less than equivalent to the pectic or pectinic acid. A few specific examples of organic derivatives prepared are given below:

Triethanolamine Salt of Pectinic Acid.—To 45 Gm. of pectinic acid (about 450 eq. wt.) suspended in 80% alcohol are added 14.9 Gm. of triethanolamine as a 20% solution in alcohol. The triethanolamine solution is added slowly with constant stirring, and stirring is continued for 15 to 30 minutes after the addition has been completed. The liquid is filtered off, the product washed with alcohol, and dried.

n-Propylamine Salt of Pectic Acid.—To 44 Gm. of pectic acid (about 220 eq. wt.) suspended in 85% acetone are added 11.8 Gm. of *n*-propylamine as a 10% solution in acetone. The *n*-propylamine solution is added slowly with constant stirring, and stirring is continued for 15 to 30 minutes after the addition has been completed. The liquid is filtered off, the product washed with alcohol and dried.

Methylglucamine Salt of Pectic Acid.—To 22 Gm. of pectic acid suspended in water are added 19.4 Gm. of methylglucamine as a water solution with constant stirring. The resultant solution of methylglucamine pectate is poured slowly into two volumes of 95% alcohol. The precipitate produced is filtered off, washed with alcohol, pressed and dried.

SUMMARY

Purified pectins (free pectinic acids) and pectic acid are pictured as typical organic acids of high molecular weight. Differences in behavior result from the differences in equivalent weight which regulate the amounts of basic reagents combining with a pectin or with pectic acid. Typical titration curves for pectins are given. Reactions with either organic or inorganic bases are described.

Triethanolamine pectate is soluble in as high as 60% alcohol, and the propyl amine in 75% alcohol.

Other interesting properties of the organic base derivatives are suggested.

REFERENCES

(1) Bonner, J., *Proc. Acad. Sci., Amsterdam,* 38 (1935), 346–359.

(2) Bonner, J., *Botan. Rev.,* 2 (1936), 475–497.

(3) Braconnot, H., *Ann. chim. phys.,* 30 (1825), 96–102.

(4) Chodnew, A., *Ann.,* 51 (1844), 355–395.

(5) Fellenberg, T. von., *Biochem. Z.,* 85 (1918), 118–161.

(6) Hirst, E. L., and Jones, J. K. N., *J. Chem. Soc.* (March 1939), pages 454–460.

(7) Olsen, Aksel G., and Stuewer, R., U. S. Patent 2,132,577 (Oct. 11, 1938).

(8) Olsen, Aksel G., *et al., Ind. Eng. Chem.,* 31 (1939), 1015–1020.

(9) Schneider, G. G., and Boch, H., *Angew. Chem.,* 51 (1938), 94–97.

(10) Shields, J. B., Mitchell, H. H., and Ruth, W. A., *J. Nutrition,* 18 (1939) 87–97.

(11) Stuewer, R. F., *J. Phys. Chem.,* 42 (1938) 305–315.

Elkonite, A Colloidal Clay*

Properties, Actions and Possible Medicinal Uses of

By M. L. Tainter, M.D., G. Kulchar, M.D., and A. B. Stockton, M.D.

Elkonite is a naturally occurring clay, laid down in terrestrial beds near Elko, Nevada. When placed in water, it swells to many times its original volume, forming a firm jelly-like mass. Accordingly, it is a hydrophilic colloid with certain characteristics that set it apart from other similar materials commonly available in medicine. This paper presents the results of a study of the scope of possible clinical applicability and usefulness of Elkonite.

EXPERIMENTAL

Physical and Chemical Properties.—In the native state, Elkonite has the appearance of a light olive-green or greyish piece of soapstone. It is rather friable, so that pieces can be broken in the hand. Dispersed through it are small particles of sand or quartz comprising something less than 5 per cent of the total mass. When a piece of this clay is put in water, the surface softens and swells, taking on a gummy gelatinous consistency. If water is added in the proportion of 6 cc. for each Gm. of Elkonite, the swelling continues for several days until finally a homogeneous colloidal gel is secured, of the general consistency of library paste. This paste quivers when the container is struck a sharp blow, thus indicating an elasticity of an organized colloidal gel. Its physical state is not affected by normal temperature changes, the paste being stable under ordinary conditions as long as the evaporation of water is prevented.

* From the Department of Pharmacology and the Division of Dermatology, Department of Medicine, Stanford University School of Medicine, San Francisco, Calif.

Less concentrated dispersions have the consistency of syrup; when still less concentrated, such as a 5 per cent concentration, the consistency and appearance resemble a greyish milk. In this low concentration, the clay solution readily passes through filter paper or cotton, leaving a sediment behind consisting of insoluble sand particles. The filterability can be used to free the Elkonite of all grit or particulate matter. Solutions can be concentrated by evaporating off the water by boiling, without destroying the colloidal nature of the clay. In fact, heating the clay to the temperature of softening of glass does not alter its characteristic physical state.

A fine non-gritty powder of Elkonite was prepared from a 4 per cent solution, which was filtered through coarse filter paper or cotton. The filtrate was collected and dried by evaporation, first on a steam-bath, and then at 110° C. for 24 hours. The resultant cake was ground in a mill to a fine powder and passed through a 100-mess sieve. This powder, or a 15 per cent paste made from it, has been used in all the tests or experiments to be described.

Chemically, Elkonite seems closely related to the general group of clays known as bentonites. However, it is much more colloidal than the bentonites known to us and comes from an area much farther west than the usual bentonite deposits. Quantitative analysis revealed the following elementary composition of the naturally occurring Elkonite:

Table I.—Composition of Elkonite

Moisture	12.83	per cent
Silica	52.70	per cent
Ferric oxide	1.96	per cent
Aluminum oxide	17.44	per cent
Calcium oxide	0.91	per cent
Magnesium oxide	3.63	per cent
Bismuth	0.011	per cent
Arsenic	Trace	
Ignition loss (moisture)	10.20	per cent
Lead, mercury, barium, fluorine, selenium and vanadium	None	

The presence of a trace of arsenic is not certain, since there was not enough in one-Gm. samples of the clay to give more than a suggestive mirror in the standard Marsh test. This suggests that any trace of arsenic which might be present is probably below the limit of physiological significance. The analytical results obtained indicate that Elkonite is essentially an aluminum magnesium silicate with small amounts of iron, calcium and bismuth present as impurities. Carbon or organic matter is not present.

The p_H of the Elkonite in 2 per cent solution was about 8.8 as judged by indicator solutions. A reading of 7.04 was obtained with a glass electrode, but this measurement may not have been reliable, since the Elkonite solution seemed to "poison" the glass electrode. In keeping with the slight alkalinity, the paste and solution taste mildy soapy, although not unpleasantly so. The material is moderately detergent, and has been used as a soap substitute under war-time conditions.

Adsorptive Power.—To determine whether the gel was an effective adsorbent for various materials, 2 experiments were performed on the adsorption of dyes. One gram. of Elkonite powder was added to 50 cc. of 1 per cent Congo red solution. After shaking for 24 hours, the colloid was separated by centrifugalization and the Congo red in the supernatant fluid estimated colorimetrically by comparison with an aliquot portion of the dye solution treated similarly, except for the Elkonite. Seventy-four mg. of the Congo red was found to be adsorbed by 1 Gm. of Elkonite. A similar test with methylene blue revealed that the Elkonite removed a 0.5-Gm. quantity of the dye so completely from the solution that less than 0.5 mg. remained in the supernatant fluid. Accordingly, definite adsorptive power of Elkonite for these dyes was demonstrated.

Because of the possible usefulness of a material of the type of Elkonite for internal administration as an adsorptive or protective agent in gastroenteritis, colitis, gastric or duodenal ulcers, etc., it was desirable to know whether it would adsorb appreciable amounts of acid or alkali and thus modify the chemical reaction in the digestive tract. To compare its action with that of other generally available colloidal adsorbent or antacid powders, 9 different substances were tested in parallel for their efficiency in adsorbing acid and alkali. The materials tried were Elkonite, Trisomin (magnesium trisilicate), bentonite, fuller's earth, Norit (an adsorptive charcoal), kaolin, bismuth subcarbonate, aluminum hydroxide and Lloyd's alkaloidal reagent. The powders were all reduced to a fineness of at least 100 mesh. Then, 1 Gm. of each substance was placed in each of 2 bottles and a suspension made by the addition of 20 cc. of distilled water. The suspension was agitated for 24 hours on a mechanical shaker and the hydrogen ion concentration determined, using an overlapping series of 11 indicators with a p_H range between 3.1 and 10.5. To one series of bottles, 1.0-cc. quantities of 1 per cent hydrochloric acid were added until the p_H of the suspension reached 3.1. To the second series of bottles, 1.0-cc. quantities of 1 per cent sodium carbonate solution were added until the p_H reached 10.5. With each 1-cc. addition of acid or alkali, the bottles were agitated for 24 hours and the p_H redetermined. This experiment was repeated a second time with close agreement. Table II contains the average values obtained. It is seen that the best antacid was Trisomin. The remaining substances were arranged in descending order of efficiency as antacids as follows: fuller's earth, bismuth subcarbonate, Norit, Lloyd's reagent, Elkonite, bentonite, aluminum hydroxide and kaolin. In order of efficiency for neutralizing alkalies Lloyd's reagent was the best, then Trisomin, Elkonite, fuller's earth, kaolin, bismuth subcarbonate, aluminum hydroxide, Norit and bentonite. One Gm. of Elkonite required 2 cc. of acid to shift the p_H to

Table II.—p_H Changes with Increasing Quantities of 0.5 Per Cent Hydrochloric Acid or 1 Per Cent Sodium Carbonate Added to 1-Gm. Quantities of Various Insoluble Powders

Substance		Control	Volume Added (Cc.) 1	2	3	4	5	6	7	8	9	10	12	13	14
Elkonite	Acid	8.7	5.1	3.1	...	...	...	...	...	...	...	...	...	...	...
	Base	8.7	9.2	10.0	10.3	10.5	...	...	...	...	...	...	...	...	...
Trisomin	Acid	8.6	8.4	8.2	8.2	7.8	7.6	6.0	5.8	5.8	5.6	5.0	4.5	4.0	3.1
	Base	8.6	9.0	9.5	9.8	10.0	10.5	...	...	...	...	...	...	...	...
Bentonite	Acid	10.5	4.7	3.1	...	...	...	...	...	...	...	...	...	...	...
	Base	10.5	...	...	...	...	...	...	...	...	...	...	...	...	...
Fuller's earth	Acid	8.8	8.5	8.3	8.3	6.8	6.5	6.1	4.0	3.1	...	...	...	...	...
	Base	8.8	9.2	9.6	10.0	10.5	...	...	...	...	...	...	...	...	...
Norit	Acid	8.8	8.3	6.5	3.1	...	...	...	...	...	...	...	...	...	...
	Base	8.8	9.6	10.5	...	...	...	...	...	...	...	...	...	...	...
Kaolin	Acid	6.4	3.1	...	...	...	...	...	...	...	...	...	...	...	...
	Base	6.4	8.6	9.0	10.5	...	...	...	...	...	...	...	...	...	...
Bismuth	Acid	9.0	8.8	8.0	7.2	6.2	4.2	4.0	3.1	...	...	...	...	...	...
subcarbonate	Base	9.0	9.6	10.2	10.5	...	...	...	...	...	...	...	...	...	...
Aluminum	Acid	9.2	3.1	...	...	...	...	...	...	...	...	...	...	...	...
hydroxide	Base	9.2	9.0	9.5	10.5	...	...	...	...	...	...	...	...	...	...
Lloyd's	Acid	9.0	6.6	5.0	3.1	...	...	...	...	...	...	...	...	...	...
reagent	Base	9.0	8.8	8.8	8.8	9.0	9.0	9.4	9.8	10.0	10.5	...	...	...	...

Table III.—Viscosity of 1-Gm. Quantities of Various Insoluble Powders in 20 Cc. Water After the Addition of Successive Amounts of 0.5 Per Cent Hydrochloric Acid or 1 Per Cent Sodium Carbonate. (All Values Are Expressed as the Ratio of the Viscosity to That of Water)

Substance		Control Before Agitation	After Agitation	Volume Added (Cc.) 1	3	5	7	9	10	11	12	13	14
Elkonite	Acid	1.41	1.91	27.00	4.96	2.04	1.26	1.51	1.33	1.33	...	...	...
	Base	1.41	1.91	1.52	1.80	2.18	2.78	2.48	...	1.77	1.66	1.57	1.48
Trisomin	Acid	1.04	1.03	1.04	1.08	1.05	1.08	1.12	1.08	...	...	...	...
	Base	1.04	1.03	1.03	1.03	1.04	1.05	1.06	1.05	...	...	...	...
Bentonite	Acid	1.51	1.71	2.03	5.81	1.63	1.76	1.51	1.52	...	...	...	...
	Base	1.51	1.71	1.63	1.53	1.49	1.58	1.40	1.40	...	...	...	...
Fuller's earth	Acid	1.03	1.03	1.03	1.03	1.03	1.03	...	...	...	...	...	...
	Base	1.03	1.03	1.03	1.03	1.03	1.03	...	...	...	...	...	...
Norit	Acid	1.03	1.08	1.08	1.05	1.06	1.05	...	...	...	...	...	...
	Base	1.03	1.08	1.08	1.03	1.08	1.06	...	...	...	...	...	...
Kaolin	Acid	1.04	1.04	1.04	1.03	1.03	1.03	...	...	...	...	...	...
	Base	1.04	1.04	1.03	1.03	1.03	1.03	...	...	...	...	...	...
$BiOCO_3$	Acid	1.03	1.05	1.05	1.05	1.05	1.04	...	...	...	...	...	...
	Base	1.03	1.05	1.04	1.04	1.05	1.04	...	...	...	...	...	...
$Al(OH)_3$	Acid	1.05	1.03	1.03	1.03	1.05	1.04	...	...	...	...	...	...
	Base	1.05	1.03	1.02	1.02	1.03	1.02	...	...	...	...	...	...
Lloyd's reagent	Acid	1.03	1.03	1.03	1.05	1.03	1.05	...	...	...	...	...	...
	Base	1.03	1.03	1.04	1.06	1.11	1.18	...	...	...	...	...	...

3.1, and 4 cc. of the alkali to raise it to 10.5. Therefore, it was intermediate in the series as far as these properties were concerned.

Effect of Acid and Alkali upon Viscosity.—The changes in viscosity of the suspensions of the same 9 substances were studied after the addition of acid and alkali, since this would reveal changes in their colloidal state as the reaction was altered.

The viscosity of the different suspensions was determined by timing the emptying of a 10-cc. pipette filled with the suspension in question, and expressing the result in terms of the time required for water. All the determinations were performed at room temperature. Suspensions of the various powders in 5 per cent concentration were made up in the same way as for the p_H determinations, and each mixture was agitated for 24 hours after each addition of fluid. Table III presents the viscosity of the solutions divided by the viscosity of distilled water as unity.

Suspensions of Trisomin, fuller's earth, Norit, kaolin, bismuth subcarbonate and aluminum hydroxide showed no viscosity changes after the addition of alkali or acid. Lloyd's reagent increased slightly in viscosity after the addition of more than 3 cc. alkali. Bentonite suspensions increased sharply in viscosity to 5.81 after the addition of up to 3 cc. of acid, but the viscosity returned to the control value after 5 cc. There were no changes after the additions of base. In contrast, Elkonite-suspensions increased markedly in viscosity to 27.0 following the addition of acid, and to 2.78, of alkali. This change was so marked with 1 cc. of acid that the fluid suspension became nearly a gel. Almost as high a viscosity was attained with the 5 per cent suspension in the presence of acid, as was seen with a 15 per cent concentration at the normal p_H value. The viscosity was also above normal until 9 cc. of the alkali had been added. Therefore, Elkonite was much more hydrophilic in the presence of acid or alkaline reactions, such as those of the gastrointestinal tract, than were any of the other materials tested.

Effect on Gastro-Intestinal Motility in Man.—Two subjects took 0.8 Gm. Elkonite powder in capsules repeatedly to determine the effects, if any, on the speed of passage of material through the gastro-intestinal tract. From 1 to 3 Gm. of medicinal charcoal were taken alone at breakfast and the time of its appearance in the feces recorded. In 8 such experiments, the average time of passage of charcoal was 11.8 hours. On 9 occasions the charcoal was taken together with 6 capsules, or 4.8 Gm. of powdered Elkonite. The average time of appearance of the charcoal was lengthened to 17.9 hours. In addition, the stools were in general of semi-solid or soft consistency, indicating a modification in physical state of the fecal material.

In one additional experiment, the progress of the same amount of Elkonite through the bowel was observed radiologically, using a small amount of barium sulfate in the capsules. There was no change in the rate of progress from that observed in normal individuals. Since the differences with the charcoals are also well within the normal range of variability, it was concluded, that, while the Elkonite may slow down the average rate of passage of material through the alimentary canal, it does not significantly affect the passage in any given individual beyond normal limits.

The main usefulness of Elkonite in the gastro-intestinal tract would seem to be as a colloidal demulcent, which could protect an irritated mucosa, and, by its gel-like consistency, give softness and bulk to the feces. In one patient, with a hyperirritable colon, the taking of one tablespoonful of the Elkonite paste with each meal for several months has been accompanied by appreciable relief of symptoms. This observation lends some support to the suggestion of its possible usefulness in this type of condition. In order to get the full effect of the Elkonite, it should be administered as the paste rather than the powder, since the powder may take 24 hours to swell to its maximum after it is brought in contact with the fluid of the intestinal tract.

Chronic Feeding Experiments in Rats.—The effect of continued ingestion of Elkonite was tested on rats, which were given the powdered material mixed with food. For this purpose, 9 albino rats weighing between 37 and 65 Gm. were divided into 2 groups and put into 2 cages. They were fed as a basic diet, the stock rat food used for our colony (1), to which was added 4 per cent barium sulfate to serve as a marker for radiologic studies. The food of the rats in one cage was medicated by adding 10 per cent of purified Elkonite powder. The food was supplied in the special all-glass feeders previously described (2), the amounts consumed being weighed at 2-day intervals. The rats were also weighed at the same time.

The average initial weights of the control rats were 59 Gm. On the 147th day, when the experimented were terminated, they weighed an average of 273 Gm. The Elkonite fed animals had an initial average weight of 54 Gm., and a final average of 250 Gm. Throughout the growth period, the weight curves of the two groups of rats ran closely parallel, the medicated animals falling within the range of the controls. Although the Elkonite rats averaged slightly lighter than the controls at the end of the experiment, there was no definite evidence of any adverse effect of the Elkonite on the nutrition of these animals, when it was fed to them for this five-month period.

The average food consumption of the control rats over the entire period was 17.4 Gm. daily for each rat. The Elkonite fed animals ate an average of 21.9 Gm. daily. When this latter value is corrected for the Elkonite present in the diet, the medicated rats ingested 19.7 Gm. daily, a value 13.2 per cent larger than the controls. Since the Elkonite rats gained no more weight than the controls, but rather slightly less, and had a larger food intake, the presence of the colloidal material interfered with the complete absorption of the food.

The distribution of the material in the alimentary canals of these rats was studied radiologically 6 times during the feeding experiment. At no time were there any evidences of alteration in motility, or abnormal distributions of the food mass, such as might be expected if balling or caking occurred. The Elkonite fed rats had clay colored stools of softer consistency than the controls, but there was nothing else that could be observed to differentiate them from the controls.

Finally, on the 147th day, all the rats were killed, and their gastro-intestinal tracts examined. In none of the animals were there any impactions or hardened masses, such as can occur when non-hydrophilic colloids are administered, and the stomach and intestines appeared entirely normal. The stomachs, small intestines and large intestines were separated, freed of contents and weighed. The average weight of the entire digestive tract in the controls was 10.28 Gm., or 3.7 Gm. per 100-Gm. body weight. The Elkonite group had an average total weight of 10.77 Gm. or 4.3 Gm. per 100-Gm. body weight. Therefore, the gastro-intestinal tracts were about 16 per cent heavier in the rats on the bulky diets than in the controls. When these differences were computed on the basis of body surface, the bulky diets produced an 11 per cent greater total weight per 100 sq. cm. of surface. The greater part of the increase was in the stomach, with a mass 19 per cent greater than the controls, while the small intestine was only 10 per cent, and the large intestine 6 per cent heavier, respectively. This effect of a bulky, high residue diet causing a work hypertrophy had been also observed by Addis (3), although he obtained somewhat greater increases with his more extreme diets.

Use as an Ointment Base.—A 15 per cent gel of Elkonite has a smooth, creamy consistency suitable for an ointment base. Any of the medicaments commonly used in the treatment of skin diseases may be incorporated with it. Ointments prepared with Elkonite as the base are homogeneous and smooth, and relatively small amounts are required for application. When rubbed on the skin, a dry film forms after 2 or 3 minutes, which holds the medicament in contact with the skin-surface. Elkonite is not rubbed off by the clothing or bed linen, but can be readily washed off with water. Since it does not spread to the hair and produce sticky smears, Elkonite makes a more satisfactory base for scalp ointments than the bases now available. The tars and dyes, which are very sticky and messy when made up in the usual ointments, with Elkonite give clean, dry adherent films, which make the treatment cleaner and less irritating to the skin, and prevent soiling of clothing.

The Elkonite gel was tried as an ointment base in the treatment of 63 patients (25 males and 38 females) with the following dermatoses: dermatophytosis, contact, seborrhœic and atopic dermatitis, pityriasis rosea, lichen simplex chronicus, scabies, impetigo, acne and pruritus ani. Salicylic acid, ichthyol, ammoniated mercury, resorcin, sulfur, naftalan, crude coal tar and its derivatives, balsam of Peru, gentian violet and oil of cade were used. The combinations and concentrations of the drugs used were those ordinarily employed in the treatment of these dermatoses. No incompatibilities were observed. The ointments were well tolerated on the glabrous skin and scalp, both in adults and infants. The response of the various dermatoses to treatment were approximately the same as with the use of the same drugs in other ointment bases. However, the improvement in the physical characteristics of the ointments was a distinct advantage.

Ointments prepared with Elkonite base maintained their consistency despite changes in temperature for a period of more than three months. They appeared to change on standing only if left in open containers from which the water of the ointment could evaporate.

SUMMARY

1. Elkonite is a colloidal clay made up mainly of aluminum magnesium silicate, is hydrophilic and swells in water. In 15 per cent concentration, it forms a gel.

2. Addition of acid or alkali to fluid suspensions of Elkonite greatly increases the hydrophilic property as shown by increases in viscosity. Some of the acid or base is adsorbed on the colloid, as shown by p_H measurements.

3. The adsorptive power for dyes and ions and the gel-like nature of Elkonite indicate that it might be a useful agent for oral administration in gastro-intestinal disorders. Preliminary trials indicate that clinical effects can be obtained, as shown by alterations in intestinal motility, and relief of symptoms.

4. Continued administration for 5 months to rats of Elkonite in 10 per cent concentration in their diet had no demonstrable influence on the rate of growth, but resulted in a definite increase in food intake over that of a parallel series of control animals. Radiologic examination and direct inspection of the gastro-intestinal tract of these rats indicated normal conditions throughout the experimental period. However, there was a work hypertrophy of the digestive tract of the Elkonite fed rats amounting to an 11 per cent increase in weight over that of the controls, being more marked in the stomach than in the intestines.

5. The most promising clinical usefulness of Elkonite would appear to be as a gel of 15% strength to be used as an ointment base. This has the following advantages over bases in common use: dries on the skin and leaves an adherent film of the medicament which will not rub off, and does not stain or smear clothing, yet can be readily removed by washing with water. The advantage of a non-greasy or sticky ointment is especially marked in applying medication to the scalp and the pubic or perineal regions.

REFERENCES

(1) Tainter, M. L., *J. Pharmacol.*, 63 (1938), 51.

(2) Tainter, M. L., *Proc. Soc. Exptl. Biol. Med.*, 30 (1933), 1234.

(3) Addis, T., *Am. J. Physiol.*, 99 (1931), 417.

Effect of Catalysts on Hydrogen Peroxide

Substances which catalyze the decomposition of hydrogen peroxide increase its germicidal effect against *Bacillus Coli*. It is reported that the addition of ferric or cupric sulfate increases the phenol coefficient of hydrogen peroxide 100 times. This effect is produced by the addition of 0.1 millimol of these salts to each ml. of peroxide.

Hydrogen Peroxide can be stabilized by the addition of certain agents, such as sulfuric acid. Urea, however, seems to be the most effective and satisfactory, although antipyrine serves almost as well.