A PHARMACEUTICAL STUDY
OF
BENTONITE

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INTRODUCTION

In compounding a prescription which contains a number of insoluble ingredients, it is essential, when the preparation is given internally, that a uniform dose results. This has always been the intent of the prescriber.

A suspending agent not only enables this uniformity of dosage but also helps to make a more elegant preparation.

Because of the importance of suspending agents in this respect and the inadequacy of substances now in use as suspending agents, this investigation of bentonite was deemed desirable.

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In the compounding and dispensing of medicaments, the problem of suspending insoluble substances very frequently arises. Precipitates are occasionally produced in mixtures intentionally, sometimes because a freshly precipitated substance is more readily assimilated than the same substance that has been previously prepared and dried and sometimes because of the liability to oxidation that is characteristic of some substances when stored for any length of time.

However, more often it is necessary to dispense insoluble substances so that when they are taken internally an equal dosage may be given and that when applied externally, the medicament is evenly distributed, promoting uniform action.

Suspending agents are substances included in a preparation to keep insoluble medicaments in a state of suspension at least sufficiently long to pour out a dose that will contain a reasonably correct portion of the insoluble matter.

In the preparation of mixtures a suspending agent is usually necessary. When no suspending agent is ordered by the prescriber, the dispenser is entitled to use his judgment as to whether one should be included, and, if so, which one.

"In general, the rule should be followed that no suspending agent should be introduced by the dispenser unless he considers that equal dosage of the insoluble substance is impossible without one."[1] In some cases the prescriber may order a suspending agent, and as a general rule the one ordered should be used.

Substances which are readily diffusible in the liquid by agitation of the bottle do not, as a rule, require the addition of an excipient to insure their uniform suspension; but other insoluble substances which are relatively much heavier than water, or are inclined to float on the surface of the liquid, demand the addition of some substance for proper diffusion. The dispenser must select the most suitable one for the particular substance.

If a mixture is dispensed containing insoluble matter, a "shake well before using" label should be placed on the bottle.

Because the extemporaneous preparation of mixtures constantly occurs, an extended use of excipients, with a view of improving the mixture, is very essential to the dispenser. Considerable skill and judgment are frequently necessary in the preparation of mextures, so that the object of the prescriber may be fully attained.

The pharmacist has many suspending agents which he may use. Probably the best manner of preparation to get the most satisfactory results lies in triturating the substance (in a very fine powder)--first to form a smooth paste, and then diluting by constant agitation. When soluble substances are prescribed in conjunction with insoluble solids, the soluble substance should be dissolved in a separate portion of the vehicle. Only sparingly or difficultly soluble substances should be powdered and mixed with the insoluble solid in the mortar before adding the vehicle.

Two of the most common suspending agents are acacia and tragacanth.

Powdered acacia should only be used for suspending when ordered. It is then best mixed with the substance to be suspended before adding the vehicle.

"Mucilage of acacia is used in quantities not to exceed one fluid dram per fluid ounce of mixture, depending a great deal on the weight of the insoluble matter. Because it forms a hard mass with the insoluble substance at the bottom of the bottle, it should not be used for bismuth salts."[2]

Powdered tragacanth usually should only be used when ordered. It is best used by placing the tragacanth in a dry bottle, adding the alcoholic liquid, shaking lightly, and then adding a large quantity of the vehicle. When mixed directly with an insoluble solid, tragacanth produces lumps on the addition of the vehicle, and such lumps are very troublesome to rub down. If any glycerin be included in the mixture, it is best to add this and triturate before adding the vehicle.

On the whole, mucilage of tragacanth is preferable to mucilage of acacia. It is used in the same proportions as mucilage of acacia.

"Compound powder of tragacanth may be used in quantities of from one to ten grains per fluid ounce of mixture. Usually not more than five grains is required. The powder is placed with the substance in a mortar, and the vehicle is gradually added with trituration. The starch present in the powder, prevents the formation of lumps. However, certain disadvantages are frequently stated. The starch produces opacity in some mixtures that should be transparent and shows as white specks in colored mixtures. It is also stated that the acacia is unnecessary in the presence of tragacanth and the inclusion of sucrose is unwarranted."[3]

"Syrup, glycerin, or honey is frequently preferable to acacia or tragacanth, especially in the case of heavy metallic salts, liable to form a compact mass which cannot be readily suspended by agitation. They are frequently used by physicians to avoid the separation of a resin. In the absence of a substance to prevent the separation of the mixture, it is the duty of the pharmacist to add some inert substance which will enable him to prepare a mixture of uniform composition."[4]

There are many substances that can be suspended. Vegetable substances, need only be rubbed to a thin smooth paste with a little of the vehicle in a mortar, and then rinsed into a bottle of known volume with more of the vehicle. An alternate method is to place the substance in a dry bottle and then add the vehicle. However, the former method seems to be the better practice. When syrup of glycerin is prescribed they are added to the insoluble substance and the vehicle is then added.

Compound powder of traganth is preferred over the mucilage in suspending bismuth compounds. Bismuth salts act by forming a coating on the interior of the intestines and suspending agents are often used to facilitate this.

Phenacetin and acetanilid are often suspended by using two to five grains of compound tragacanth powder per fluid ounce of mixture.

In the case of gum resins--ammoniacum, golbanum, gambage, myrrh, and scammonium--these do not require a suspending agent because the gum present is sufficient to suspend the resin they contain. They should be powdered in a mortar and then triturated with some of the vehicle. The resulting suspension must be strained through earthy matter which often accompanies the commercial drug.

When tincture of asofetida, guaiac, lupulin, myrrh, and similar substances are placed in combination with aqueous saline liquids, separation of the resinous matter will invariably result unless a protective agent is present, by means of which the finely divided precipitate is kept in perfect suspension. Examples of these might be:

"Rx

Potassii Bromidi	ʒiv
Tincture of Lupulini	℥i
Aquae Menthae Vir.	℥ii

Rx

Potassii Chloratus	℥ii
Tincture of Guaiaci	℥i
Aquae .... q. s. ad.	℥iv

Mix the resinous tincture with powdered tragacanth in a mortar. Then add the water with constant stirring. A perfect mixture can be obtained. In these prescriptions ten or twelve grains of tragacanth is sufficient. As a rule ten grains of tragacanth is required for each flued ounce of a tincture or one-half fluid ounce of a fluidextract.

Using honey with resinous tinctures may be illustrated by the following prescription.

Rx

Potassii Chloratia .... ℥i
Tincturae Guaiaci
Tincturae Cinchonae Co. .... a.a. ℥ss
Mellis
Aquae .... q. s. ad. ℥iii

Place the honey in a mortar and slowly add and mix the tincture of guaiac slowly, add the potassium chlorate dissolved in one and one-half fluid ounces of water, mixing well, and add the compound tincture of cinchona last, a uniform mixture of a pink color results."[5]

All powerful remedies such as mercuric chloride, arsenic trioxide, the salts of morphine, and strychnine should always be brought into a state of perfect solution before they are added to the other ingredients of a mixture: This insures a uniform distribution throughout the liquid.

Because of the great importance of suspending agents in pharmaceutical dispensing, the use of bentonite, a clay-like material has been of great interest and value as a suspending agent.

Many definitions and descriptions of bentonite have been given by various authors, but probably the most satisfactory one thus far produced is that by Ladoo. He states that bentonite is "a group or series of clay-like materials characterized by an alkaline earth content of from five to ten per cent, fine, grain size, high adsorptive powers, and usually very strong colloidal properties."[6]

Bentonite in the ground is usually damp. It is then a green, soft, wax-like material with a high luster. On drying the luster disappears and the material becomes harder and lighter in color. The fracture is conchoidal. The surface of a weathered outcrop is white with a crinkly, coral-like appearance. Gypsum crystals up to three inches in lenght are often contained in the bentonite. These crystals weather out and are abundant near the outcrop.

Bentonite was first produced in Wyoming in 1888, when William Taylor shipped a small amount from Rock Creek. The price was twenty-five dollars per ton then.

The origin of bentonite has been the subject of much discussion and many theories concerning its origin have been advanced. The rock name, bentonite, is usually restricted to a material derived from volcanic ash. This restriction was placed on the term because the physical properties of bentonite depend on inherited structure as much as on mineral composition.

The process involved in the alteration of ash to bentonite is not well known. Ross Miser and Stephanson have produced evidence to show that the alteration took place after deposition. They also list several known factors involved in the alteration process. The factors listed are the absence of oxidation conditions, the presence of water for hydration, the removal of excess chemical constituents, and the probable presence of bicarbonates, sodium chloride and a possibility of magnesium salts from the sea water. They say "alteration seems to have been the result of hydration and solution of an unstable gloss that was perhaps more or less aided by the presence of chlorides and bicarbonates, the latter probably in very weak concentration."[7]

The United States Geological Survey has defined bentonite as "a transported stratified clay formed by the alteration of volcanic ash shortly after deposition."[8] Spence agrees that the source of the material was volcanic ash, but believes that in some cases the clay has not been transported, or in other words, there has been no transportation of the clay material after the alteration of the volcanic ash took place.

Its mode of occurence and certain of its features clearly indicate that it represents a decomposition product of volcanic ash. The evidence comprises such things as the essential absence of quartz (which is present in all ordinary clay sediments), the presence of feldspar, and the extension of individual beds, often very thick ones, over vast distances without important variation in thickness. The clayey matter in normal sediments has been so acted on by electrolytes and other active substances that it has lost its original porosity and tendency to take up water, accompanied by swelling, which bentonites exhibit to such a marked degree. The chemical composition of the bentonite is, moreover, exactly what would be expected from the partial alteration of an intermediate igneous rock, accompanied by the removal of alkalies and addition of water.

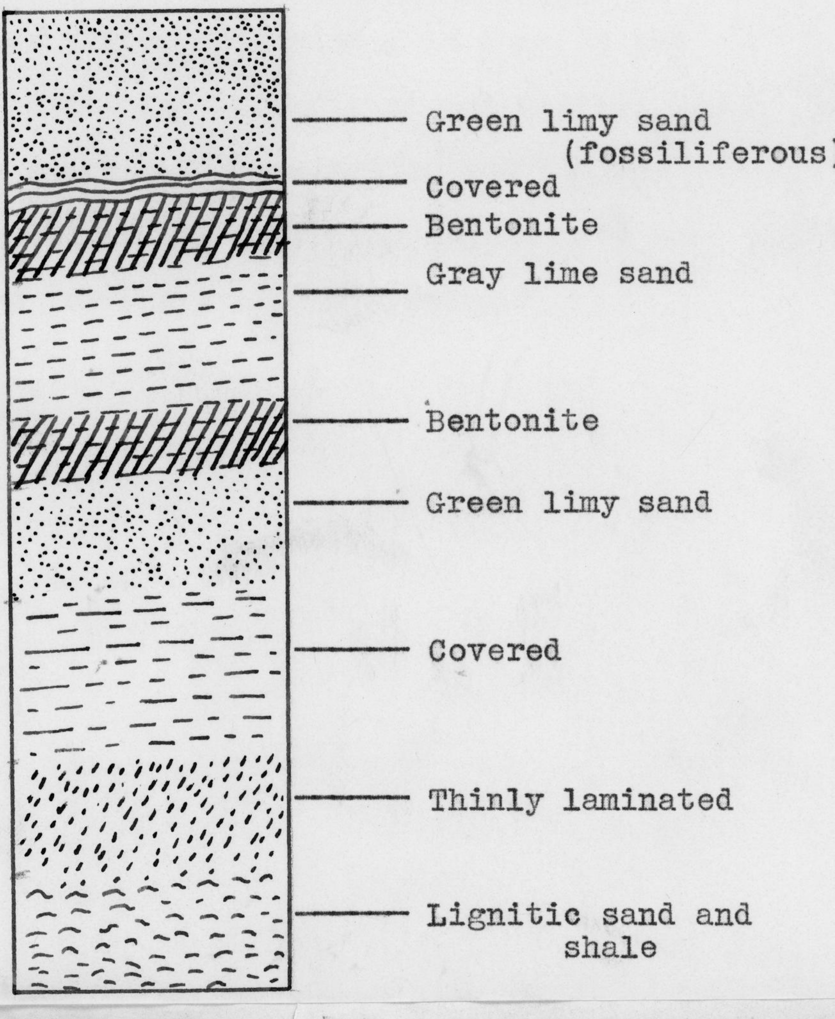
"A volcano explodes and sends up into the air a vast body of pulverized, glossy lava, which is carried off by the winds and deposited in strata, for the most part thickly near, but thinly even hundreds of miles from the source. In the cases of the South Dakota and Wyoming deposits, the sources were probably in the middle Rocky Mountains; in that of the Tennessee deposits, the volcano seems to have been under the present Cumberland Plateau. With this lava dust are carried more or less hydrochloric acid, hudrofluoric acid, sulfur dioxide and perhaps other corrosive gases. These attack the surfaces of the particles of lava, rendering them open to relatively rapid disintegration by such weathering agencies as may affect them."[9]

The original lava is glossy and amorphous, and the first product of weathering or disintegration is likewise amorphous, but consisting largely of alumina and silica in partially hydrated form, it also possesses many of the properties of colloids. "In time the colloidal gel starts to become crystalline, a large number of nuclei developing in it and crystal material building around these nuclei until the whole mass is occupied by minute crystaliine grains in contact with one another; it is then of the character to which the name 'metacolloid' has been assigned--i.e., a colloid which has become crystalline in place, without intervening solution and recrystallization. Such colloids turned into metacolloids are common among minerals--for instance, chalcedony, limonite, psilomelane, and many clays."[10]

"The nature of the crystalline substance depends on the original composition of the colloidal gel. In the case of the better known deposits of bentonite, the lava seems to have been originally of intermediate composition--that is, containing sixty to sixty-five per cent of SiO_2 and twenty to twenty-five per cent of $Al_2O_3 + Fe_2O_3$. In the resulting colloid the ratio of Al_2O_3 to SiO_2 is near 1:2."[11]

"In Mississippi the bentonite occurs in layers interstratified with the Eutaw sands of the Upper Cretaceous Age."[12]

"A general section showing the stratiographic relation of bentonite may be shown by the following diagram:"[13]



The principal commercial deposits of bentonite are found in South Dakota, Wyoming and California, but there are deposits of varying size and quality in Tennessee, Texas, Arizona and some of the western provinces.

The commercial value of a bentonite deposit depends upon (1) the type or class of bentonite, (2) the thickness of the seam, (3) the dip of the seam, (4) the amount of overburden, and (5) the transportation costs.

Mining bentonite is mostly done by stripping the overburden and breaking up the beds with plows, although in some sections where the overburden is fifty to one-hundred feet, the main haulage ways are timbered. The bentonite in some cases is hauled twenty-five miles to mills. As the bentonite freezes in the winter, all mining is done in the summer and large stock piles are accumulated for winter milling. "To show the increase in production and the increase in value of bentonite, the following figures are presented. They are given for the state of Wyoming."[14]

Year	Short Tons	Value in Dollars
1921	433	2, 155
1922	466	7, 313
1923	614	10, 448
1924	23,716	41, 172
1925	2,584	63, 657
1926	4,409	98, 853
1927	7,498	121, 146
1928	22,918	383, 970
1929	22,053	190, 156
1930	25,006	249, 765
1931	16,080	143, 969
1932	12,632	107, 567
1933	21,306	166, 630
1934	27,161	246, 548
1935	34,415	350, 846
1936	55,090	520, 852
1937	67,958	659, 111

The so-called bleaching clays are of two distinct types: naturally active and activable. A naturally active bleaching clay has physical properties that give it a capacity for decolorizing or clarifying (bleaching) oils and fats. Clay of this type is generally known as fuller's earth.

Activable clay is a natural substance which, through a process of partial acid leaching acquires physical properties that make it a highly active bleaching agent for oils. The most powerful of the bleaching clays are of this type. Although not all so-called "bentonites" are rendered active by chemical treatment, yet it is the bentonite clays that provide our most efficient activable clays.

The bentonites produced in the United States are divided into two classes: (1) those which swell to several times their original volume when in contact with water and (2) those which swell no more than ordinary plastic clays. Improved grades of bentonite have been placed on the market so that when employing these powders it is now unnecessary to wait until the coarse particles separate from a bentonite suspension before using it in lotions. For pharmaceutical use and the manufacture of cosmetics the grade sold as "Wil-Kinite A. S." is very good to use. This is air-floated and its grit content is negligible. On account of the present shipping arrangements, supplies of "Wil-Kinite" are difficult to obtain, but it is hopeful that a new stock will soon be available.

Physically bentonite is called a detergent colloid, suspensoid and emulsifier. Ninety per cent of the dry particles are less than one micron in size and all are less than five microns. In solution eighty-nine per cent of the particles are less than one-tenth of a micron.

"Under a single nicol prism the material is ultra-microscopic. No individual grains can be seen, and practically the whole section appears as a uniform light orange colored mass. The only exceptions are very small inclusions, which are chiefly quartz, magnetite and opatite. These minerals are probably foreign to the bentonite, having become trapped in the bentonite when it was deposited.

The index of refraction is slightly below 1.541. Under crossed nicols the material is isotropic with the exception of the very few inclusions, and also a small amount of secondary calcite appearing along the cracks cutting the section. The main isotropic mass shows no hint of structure. According to the investigations of Ross and others, the chief minerals constituent of bentonite is Leverrierite."[15]

"The term thixotropy, first used by Peterfi, refers to an isothermol, reversible gel-sol transformation by means of shaking or other mechanical influences. The thixotropy of bentonite dispersion depends on the diameter of the container as well as the concentration of the dispersed substance. Thixotropic properties of bentonite disappeared after dialysis, but could be restored by the addition of electrolytes. Ultramicroscopic examination of dialyzed bentonite dispersions of low concentration showed that addition of electrolytes first removed the translational, next the rotational component of Brownian motion. Further addition caused aggregation and coagulation."[16]

The chemical analysis of bentonite varies slightly with the investigator. H.W.Kerr of the University of Wisconsin states that bentonite is a mexture of at least two minerals which are difficultly separable by mechanical means because of the colloidal properties of the substance. "It was found possible to decompose the active material of bentonite by boiling for eighteen hours with normal hydrochloric acid. The liberated silicic acid was then extracted with a ten per cent solution of sodium carbonate. The analysis of these extractions showed the ration of Al_2O_3 to SiO_2 was almost one to six. By further consideration of the base-exchange reaction for cations of different valence, it was shown that the active aluminosilicic acid was monobasic, and when due allowance was made for the unsaturation of the compound, the analysis calculated from the free acid agreed fairly well with the formula: $H_2O\ (Al_2O_3 \cdot 6SiO_2) \cdot 8\ H_2O$. By leaching a sample of bentonite with 0.1 NHCl and washing the sample with water, the free acid was precipitated. This acid suspended in water gave a pH of 2.73. It is suggested that the compound described is of widespread occurrence in soils and for those which are non-alkaline is possible the predominant if not the only mineral in their inorganic exchange complex."[17]

Freeman in a paper presented at the American Pharmaceutical Association meeting states that "bentonite is a mineral clay compound composed of ninety per cent aluminum, iron, magnesium hydrate which acts as an emulsifier for fixed oils, and liquid petrolatum, a suspensoid for insoluble powders such as talc, starch, zinc oxide, and bismuth salts, and a detergent colloid."[18]

Other chemical descriptions given state that bentonite is a clay material which contains seventy-five per cent or more of the crystalline minerals montmorillonite, $(Mg.Ca)\ O \cdot Al_2O_3 \cdot 5\ SiO_2 \cdot nH_2O$, or beidellite, $Al_2O_3 \cdot 3\ SiO_2 \cdot nH_2O$. Another investigator states that it consists of the hydrous silicates of aluminum, magnesium, and calcium; small amounts of iron are also present. The analysis corresponds to the formula:

$(Mg\ Ca)\ O \cdot Al_2O_3\ 5SiO_2 \cdot nH_2O.$

From the above we see that they compare favorably.

"In an investigation made by W.F.Hand, State Chemist of Mississippi, the crude sample was air dried for several weeks. The sample had been obtained in the field by digging as far back from the outcrop as possible in order to obtain material uncontaminated from slump and surface waters."[19] This analysis showed:

SiO_2	60.51%
Al_2O_3	16.56%
Fe_2O_3	7.74%
Volatile matter ...	14.34%
Total	99.15%

Probably almost the whole amount of the volatile matter is water, because as stated above, the specimen was collected fairly close to the outcrop. It is also believed that the iron content as shown is higher than would be the case in absolutely fresh material.

An analysis of a sample of bentonite from Bell Foursche, South Dakota compared to other deposits, shows the following:

Constituent	Bell Foursche	Other deposits
SiO_2	60.64	54.00
Al_2O_3	23.23	11.84
Fe_2O_3	3.92	3.97
CaO	0.59	4.94
MgO	2.19	3.24
Na_2O	4.33	0.66

(The balance is water and small amounts of other constituents.)

An analysis of average bentonite in Wyoming, which is the standard for the United States shows:

SiO_2	61.94
Al_2O_3	15.97
P_2O_5	0.07
Fe_2O_3	2.92
FeO	0.71
MgO	2.45
CaO	1.72
Na_2O	1.61
K_2O	0.29
H_2O-	7.17
H_2O-	3.95
TiO_2	0.23
CO_2	0.41
SO_3	0.15
S	0.01
C	0.14-

In comparison, a Mississippi sample of bentonite was reported to contain:

	1	2	3	4	5	6	7	8
SiO_2	60.51	60.68	67.04	59.80	60.18	66.90	59.84	54.00
Al_2O_3	16.56	15.66	13.46	16.38	26.58	15.26	11.84	24.48
Fe_2O_3	7.74	6.40	2.79	2.23		2.80	3.26	3.00
FeO		none	0.23	3.52		0.12		
CaO		0.29	1.78	1.82	0.23	0.46	2.90	2.08
MgO		1.79	1.93	2.67	1.01	2.26	2.32	2.75
Na_2O			0.53	2.00		2.12	2.13	1.74
K_2O			0.22	0.27	1.23	0.42	2.34	
TiO_2		1.00	0.25	0.05		0.11		
P_2O_5			0.09	trace		0.04		0.71
S			0.01	nil		0.01		
SO_3			nil	nil		0.08	loss	
C			0.10	0.09		0.03	on ignition	
CO_2			0.02	0.72		0.05	10.50	
H_2O-	14.34	5.56	6.64	5.18	10.26	5.80		9.12
H_2O		6.18	4.92	4.91		3.67		
	99.15	97.52	100.01	99.62	99.49	100.13	95.13	97.88

There has been much discussion as to the way in which the main constituents, silica, alumina, and water are combined in the bentonite. Until a relatively recent date, bentonite has been thought of as composed of colloidal material. It was believed that it was the colloidal character of the material that gave it its unusual properties. Recent investigations carried on chiefly by various members of the United States Geological Survey, the Geophysical Laboratory, and the United States National Museum, have tended to disprove this and show the material is crystalline, composed of a definite material known as Leverrierite.

Bentonite occurs in massive beds and is devoid of stratification. The material is hard and tough, so that a dry piece can hardly be broken between the fingers. It is more resistant to weathering than the surrounding sand and consequently the outcrop in the creeks causes small waterfalls to be formed. There is a total absence of grit, and the material is so fine-grained that with a lens no individual grains can be differentiated. It has a distinct soapy feel.

The weathered material is greenish-gray in color, and considerably iron-stained along the cracks and crevices. The conchoidal character is better shown by the weathered material than the unweathered. Many large rounded masses can be seen that are built up of concentric layers from a fourth to one inch thick. If such a mass is broken, it appears similar to a very large onion that has been cut in two. This is a very pronounced character of the material. Material that has been air dried will absorb from two to four times its volume of water and increase correspondingly in size. The material has no grit and can be crushed into a powder practically all of which will pass through a number two mesh sieve. Material of this fineness will form a suspension in water that will stand for a long time (several days) without settling out. Blocks of the material when soaked in water will form a jelly-like mass about the consistency of a thick paste, that appears to stay almost permanently in this condition.

Pulverized bentonite is fine grained, light colored, dark or black. After firing, the color is white, buff or brown. The fracture may be conchoidal, peaty or shale-like or none at all. Its affinity for water is strong, it being able to absorb up to ten times its volume with a consequent increase in bulk.

Often times the color is gray or pink, depending upon the nature of the impurities.

"Colloidal properties are attributed to a felted texture and micaceous structure in which the crystals have appreciable size in two dimensions. In the four types of bentonite studied, the relative amount of swelling in water was found to be a rough method of classification. The swelling may be controlled by the addition of sodium chloride but other salts also affect the swelling as well as the hydrogen ion concentration. Heat destroys the colloidal properties of the mineral. Regulated heat treatment differentiates the bentonites in the same order as does the water swelling.

Nelson has classified commercial bentonite into the following classes:"[20]

1. Alkaline bentonite containing easily replaceable alkaline bases and having original properties not permanently destroyed with sulfuric acid.
2. Alkaline bentonite same as number one except having original properties permanently destroyed with sulfuric acid.
3. Alkaline earth bentonite same as number one except for containing alkaline earth instead of alkaline bases.
4. Alkaline earth bentonites the same as number two except containing alkaline earth instead of alkaline bases.

A prominent characteristic of this nonrefractory clay is then, its colloidal nature and its ability to adsorb water with consequent diffusion through the liquid formation of a slippery jell. We may term the particles as "one-demensional colloids" which account for the enormous powers of water absorption and swelling.

There is a variation in the colloidal properties of the clay, depending upon the area from which it is obtained. Tennessee samples are practically noncolloidal. Wyoming and California samples exhibit under the ultramicroscope a large percentage of particles of colloidal dimensions, showing active Brownian movement. Areas which contain bentonite deposits show a curious aspect because after a rain they become covered with a thick mass of very slippery jelly, and on exposure to air, they soon shrink again and during dry weather are fluffy.

Because of its unusual properties, bentonite appears to have a great potential importance in a wide variety of industries. One of the first uses of bentonite was for stuffing horses hoofs, and it was sold under the name of White Rock and the like. When it is made up into a jelly with water, it forms a cataplasm, or poultice that has great power in reducing swellings and inflammation, and draws the soreness from the horse's foot. It has been used to advantage in cases of rheumatism and seems to act similarly to the so-called "fango" baths or mud baths, for which many people go to Europe. It has some value as a beauty clay and is said to be the basis of the proprietary poultice material called antiphlogistine.

Commercially, bentonite in the manufacturing of ceramics has large possibilities. It may be used to suspend enamels. "Since a small percentage of colloidal clay will markedly affect the properties of a soil, it seems that only a little bentonite is needed in most pottery mixtures, therefore the use of larger amounts than are demanded will cause trouble. It should also aid soils that are deficient in colloidal matter."[21]

Bentonite can also be used as a filler for soap. It gives toilet soap a particularly velvety feel and, judging from the fact that clay soaps were widely used in Germany during the World War I, it must have some detergent value. Its value must be worked out in each case, but from the fact that it has great adsorptive powers and that its particles have active Brownian movement, there is some basis for the claim that it aids in laundry soap.

"According to the Bureau of Mines, experiments at the Forest Products Laboratory seem to show that the addition of small amounts of bentonite to the clay used in filling paper greatly increases the percentage of clay held by the finished paper. Some of the results:

Clay	Bentonite	Retention
90%	10%	54%
80%	20%	64%
0%	100%	84%

It is said that the bentonite gives a superior feel to the paper and because of its smoothness it should be valuable in paper-coating mixtures."[22]

Bentonite is used for de-inking newspaper. It absorbs the ink without affecting the pulp. Because it readily absorbs many aniline colors, it can be used as a color base or as an addition to other bases and can be used in paints and calcimines.

This substance has been found to be an excellent retarder in plaster of Paris, but on trial it was found to increase the speed of set of a commercial plaster of Paris, possibly because it adsorbed the organic retarder thus contained.
It is used as a good binding material for electrical and chemical porcelain, graphite crucibles and abrasive wheels.

Some varieties when burned and granulated, are used as water softeners, acting as zealites.

In the refining of petroleum, certain varieties have shown sixteen times the efficiency of fuller's earth for this purpose. The patents cover only the clay by washing, treating with sulfuric acid and drying; thus removing the alkalies, alkaline earths and some of the alumina, leaving a residue of very fine grains of silicate.

As an emulsifier and protector, it would serve for emulsifying cutting oils, stuffing oils for leather and many similar substances. Kirschbraun emulsifies it with asphalts and pitches. These emulsions may be used as paints, for roofing, for the protection of structural steel and the like. Walker writes that a six per cent bentonite in water gel will in most instances make a nice emulsion, and that is about as high a concentration of bentonite that will remain fluid.

Among other things, the use of bentonite has also been mentioned for use in the dye industry because of its absorbent properties, in explosives as an absorbent for nitroglycerin, in refining oils and fats, in putty, in horticultural sprays and animal dips to form a permanent suspension, in lubricants because of its excessive smoothness, in pencils and crayons because of fineness and lack of grit, and at present it is the base for many beauty muds. Many cosmetics and special soaps contain this substance. "Cox at the United States Pharmacopoeial Preconvention meetings in Washington suggested the use of bentonite (10%) with glycerin and magnesium sulfate to be used as a wet compress."[23]

Work done on bentonite has proven that therapeutically it is safe internally and externally. Dr. Fantus'[24] experiments have proven it nontoxic to rats.

"In the preparation of simple aqueous gels the bentonite is sprinkled on the surface of the water, and after a few minutes the medicaments are mixed; alternatively, the product may be triturated in a mortar, the water being added gradually and the paste frequently removed with a flexible spatula from the sides of the mortar. Two gels with different characteristics are prepared as follows:

	A	B
Bentonite	2 Gm.	5 Gm.
Water	30 Gm.	20 Gm.

A has the apparent consistency of glycerin; B is a greyish-white in color and has the consistency of anhydrous wool fat and appears greasy to the touch; it can be spread easily on the skin, where it dries rapidly, leaving a thin scarcely perceptible layer of clay, which can be removed instantly by simply washing with water."[25]

From work published in the Fournal of the American Pharmaceutical Association bentonite is useful only for the suspension of alkaline insoluble substances, for example, chalk. "All the acid lotions, such as lotions of lead and opium, white, yellow and black wash that have a pH of about 6.0 are incompatible with bentonite pH 8.0 which not only does not prevent sedimentation but even causes precipitation. It is undoubtedly a question of electric charges. True acids, including organic acids such as benzoic acid are also incompatible. On the other hand, carbolic acid, phenol, not being a true acid is compatible."[26] The journal goes on to state that 0.1 gram of bentonite adsorbs 0.35 gram of methylene blue, that is, one-third of its weight, but there is no appreciable absorption of eosin.

The usual stock solutions that were used were six per cent aqueous solutions and the same strength with lime water. The bentonite should always be added to the fluid and the best results were obtained using milk shakers and by agitation in a bottle. The lime water bentonite solutions separate into two layers, the supernatant or upper layer equivalent to about ten per cent of the total volume is clear.

Of much value is the work which has been done with bentonite in suspending calamine lotion. "It is a remarkable fact that calamine lotion, first used in 1907, has become one of the leading preparations, in point of usage, of the N.F. as shown by the Gathercool report from which we learn that, from a usage of 12.5 per 10,000 prescriptions in 1926, it has more recently been called for in 44 prescriptions per 10,000 and the total prescription usage of calamine in all its forms amounted to 95 per 10,000 prescriptions. Even though it is freely admitted that calamine lotion may have other virtues than the fact that it is somewhat skin-colored, we have taken the proposition for our thesis that skin-colored ("cuticolor") preparations should, in general, be preferred in dermatology to those with other colors, and that the use of skin-colored preparations is mandatory, so far as possible, on surfaces of the body exposed to view."[27]

"For the stabilizing of calamine lotion, gums have been tried and found wanting. When two per cent acacia is used, there is a tendency for it to produce a cement-like sediment on standing, which cannot be incorporated by shaking. Tragacanth (1%) and karaya (½%) do not keep the material in suspension for any length of time. The general disadvantage of gums is that they are prone to ferment ation and that on drying they leave a sticky film behing."[28]

A formula for an improved calamine lotion published in _The Pharmaceutical Journal_[29] was given as follows:

Cuticolor powder ...	15.0 Gm.
Bentonite	2.5 Gm.
Rose water	to 100.0 cc.

A bentonite solution was prepared with the rose water. To the cuticolor powder in a mortar, the bentonite solution is added in portions, triturating after each addition.

In the above formula, lime water should not be used in place of rose water because when lime water is employed more than five per cent bentonite is required. This is due to the alkalinity of the solution, and the same degree of separation is obtained with sodium hydroxide solution of the same pH (approximately 10). Thus bentonite is useful only for the suspension of alkaline insoluble substances.

The following chart shows the amount of sedimentation in certain combinations, with and without bentonite.

Distance of the upper surface of the sediment from the surface of the fluid after standing for the specified time:

			15 min.	30 min.	45 min.	60 min.	75 min.	24 hrs.	96 hrs.
1.	Zinc oxide Water	1.6 to 10.0	5mm.	15mm.	23mm.	23mm.	23mm.	32mm.	32.mm
2.	Calamine Water	1.6 to 10.0	21mm.	25mm.	30mm.	30mm.	30mm.	34mm.	34mm.
3.	Calamine Zinc oxide Water	0.8 0.8 to 10.0	17mm.	21mm.	28mm.	28mm.	28mm.	33mm.	33mm.
4.	Bentonite Water	0.3 to 10.0	0mm.	0mm.	0mm.	0mm.	0mm.	0mm.	0mm.
5.	Calamine Zinc oxide Bentonite Water	0.8 0.8 0.1 to 10.0	1mm.	5mm.	6mm.	6mm.	7mm.	19mm.	21mm.
6.	Calamine Zinc oxide Bentonite Water	0.8 0.8 0.2 to 10.0	0mm.	0mm.	1mm.	1mm.	2mm.	5mm.	14mm.
7.	Calamine Zinc oxide Bentonite Water	0.8 0.8 0.3 to 10.0	0mm.	0mm.	0mm.	0mm.	0mm.	0mm.	1mm.
8.	Calamine Zinc oxide Calcium hydroxide	0.8 0.8 to 10.0	25mm.	29mm.	30mm.	30mm.	30mm.	33mm.	34mm.
9.	Calamine Zinc oxide Bentonite Calcium hydroxide	0.8 0.8 0.3 to 10.0	5mm.	9mm.	10mm.	10mm.	12mm.	18mm.	19mm.
10.	Calamine Zinc oxide Karaya Water	0.8 0.8 0.05 to 10.0	7mm.	11mm.	12mm.	15mm.	15mm.	33mm.	36mm.
11.	Calamine Zinc oxide Tragacanth Water	0.8 0.8 0.1 to 10.0	8mm.	10mm.	10mm.	10mm.	12mm.	15mm.	20mm.
12.	Calamine Zinc oxide Acacia Water	0.8 0.8 0.2 to 10.0	0mm.	1mm.	2mm.	2mm.	3mm.	24mm.	53mm.

The high degree of colloidality of bentonite is shown by line four: there being no sedimentation even after days of standing, excepting for some coarse particles contained in the bentonite--but even this will not happen in a good grade of bentonite.

"When we add bentonite to calamine lotion in increasing quantities we find that one per cent (line five) and two per cent (line six) are not quite sufficient to stabilize it; but three per cent (line seven) does so, providing distilled water or rose water is used. When lime water is employed (line nine) the lotion sediments to eighteen millimeters below the surface level after twenty-four hours (by th chart). The bentonite also adds body to the lotion. It requires more than five per cent of bentonite to stabilize the lotion in the presence of calcium hydroxide. That it is not the calcium but the alkalinity which is responsible for the sedimentation noted is shown by the fact that sodium hydroxide solution of the same degree of alkalinity (pH approximately 10.0) produces the same separation.

The conclusion thus offered is that calamine lotion can be improved by the addition of a 2.5% solution of bentonite."[29]

Recent work has been done by Hubbard and Freeman. In their experiments they state: "Volclay Grade A finest bentonite was used. It is grit free and ninety per cent of the particles are one micron, the balance not more than five microns. In aqueous suspensions the particles become one-tenth micron. A six per cent solution has a pH less than ten. In all cases the bentonite is added to the water or lime water in a rotating electric mixer, producing a uniform suspension immediately, superior to that secured by bottle agitation. Never add water to bentonite or mix by trituration in a mortar. Stock solutions of six per cent bentonite in both water and lime water were prepared and those were used for the insoluble powders. The powders are added to bentonite."[30]

The work done by these men was on the following prescriptions:

Bismuth subcarbonate	20.0
Bentonite 6% (aqueous or lime water q. s.)	90.0

Place the bentonite suspension under a rotary electric mixer and add the bismuth subcarbonate.

Starch	2.0
Bismuth subcarbonate	20.0
Bentonite in aqueous or lime water--6%	90.0

Place the bentonite suspension under a rotary electric mixer, add starch, then bismuth subcarbonate.

Bismuth subnitrate	20.0
Bentonite in aqueous or lime water	90.0

Place the bentonite suspension under a rotary electric mixer and add the bismuth subnitrate.

Starch	2.0
Bismuth subnitrate	20.0
Bentonite in aqueous or lime water	90.0

Place the bentonite suspension under a rotary electric mixer, add starch, then bismuth subnitrate.

Zinc oxide	5.0
Talc	5.0
Sodium borate	5.0
Menthol	1.4
Alcohol	15.0
Bentonite in lime water--6%	100.0

Place the bentonite suspension under a rotary electric mixer, add the talc, then the zinc oxide, the sodium borate, and finally dissolve the menthol in alcohol.

Precipitated sulfur	3.0
Spirit of camphor	5.0
Stronger rose water	15.0
Bentonite in lime water--6%	60.0

Introduction to Experimental Work

The experimental work consisted of preparing mixtures of insoluble powders such as compound chalk powder and calamine with suspending agents such as acacia, tragacanth, and bentonite, and allowing the preparation to stand for a period of time. Comparisons were then made by observing the degree of "settling out" of the insoluble powder during this length of time. The preparations were also observed under the microscope and a comparison was made as to the relative degree of subdivision of the insoluble powder in the mixtures.

A comparative study of the suspending power of bentonite, acacia and tragacanth was carried out using compound chalk powder U.S.P. XI as the insoluble powder to be suspended. A comparison was made to the official preparation misturae cretae compositus.

Compound chalk powder of the U.S.P.XI contains:

Prepared chalk	30 Gm.
Acacia, in very fine powder	20 Gm.
Sucrose, in fine powder	50 Gm.
To make	100 Gm.

Chalk mixture in the U.S.P.XI is prepared as follows:

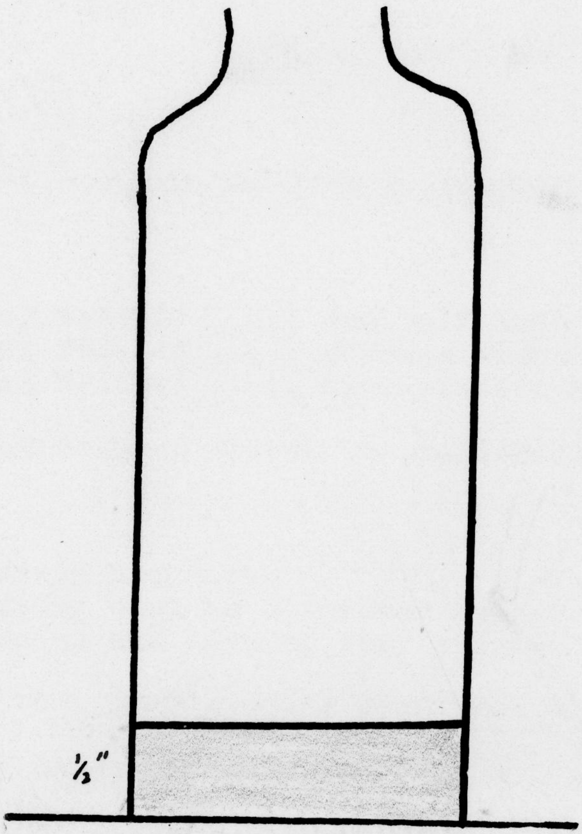
Compound chalk powder	20 Gm.
Cinnamon water	40 cc.
Distilled water, a sufficient quantity	
To make	100 cc.

Gradually add the cinnamon water and about 20 cc. of distilled water to the compound chalk powder in a mortar, triturating until the mixture is uniform; transfer this to a graduated vessel, rinse the mortar with enough distilled water to make the product measure 100 cc. and mix thoroughly.

Results:

The mixture upon standing a short time settles out completely. The sediment is one-half inch.

Compound Chalk Powder



Acacia

Procedure:

The following technique was used in preparing the mixtures containing acacia:

The compound chalk powder was mixed intimately with the powdered acacia. Distilled water was slowly added with constant trituration. It was then made up to the specified volume.

Results:

Upon standing five hours, sedimentation occurred as follows:

A. 1% acacia (total volume) ..... one-half inch
B. 3% acacia (total volume) ..... seven-sixteenths inch
C. 5% acacia (total volume) ..... nine-sixteenths inch

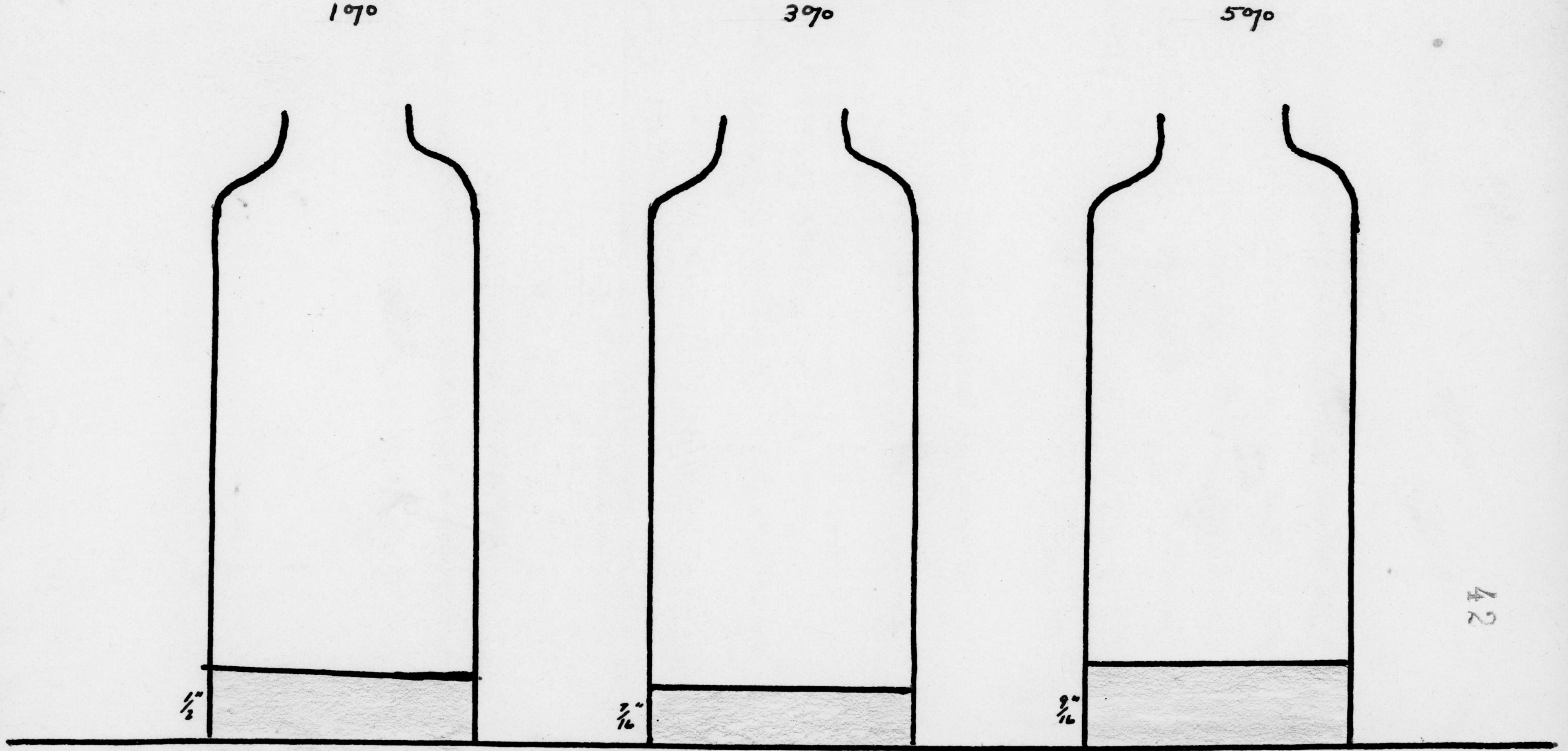
Observations under the microscope showed the following to be true:

A. 1% ..... coalescing had begun
B. 3% ..... coalescing even to a greater extent
C. 5% ..... coalescing and lumping very evident

These observations were more or less confirmed when it was found that the above solutions were somewhat difficult to shake into a uniform suspension, indicating a clumping or solidifying of the insoluble powders.

Compound Chalk Powder

Suspending Agent-Acacia



Tragacanth

Procedure:

The powdered tragacanth is wet with a small amount of alcohol in order to prepare a uniform mucilage. To it a small amount of the vehicle is added, then the compound chalk powder with constant trituration. The product is then made up to the desired volume.

Results:

Upon standing five hours, sedimentation occurred as follows:

A. 1% solution (total volume) .... 1 inch
B. 3% solution (total volume) .... 2 3/8 inch
C. 5% solution (total volume) .... 3¼ inch

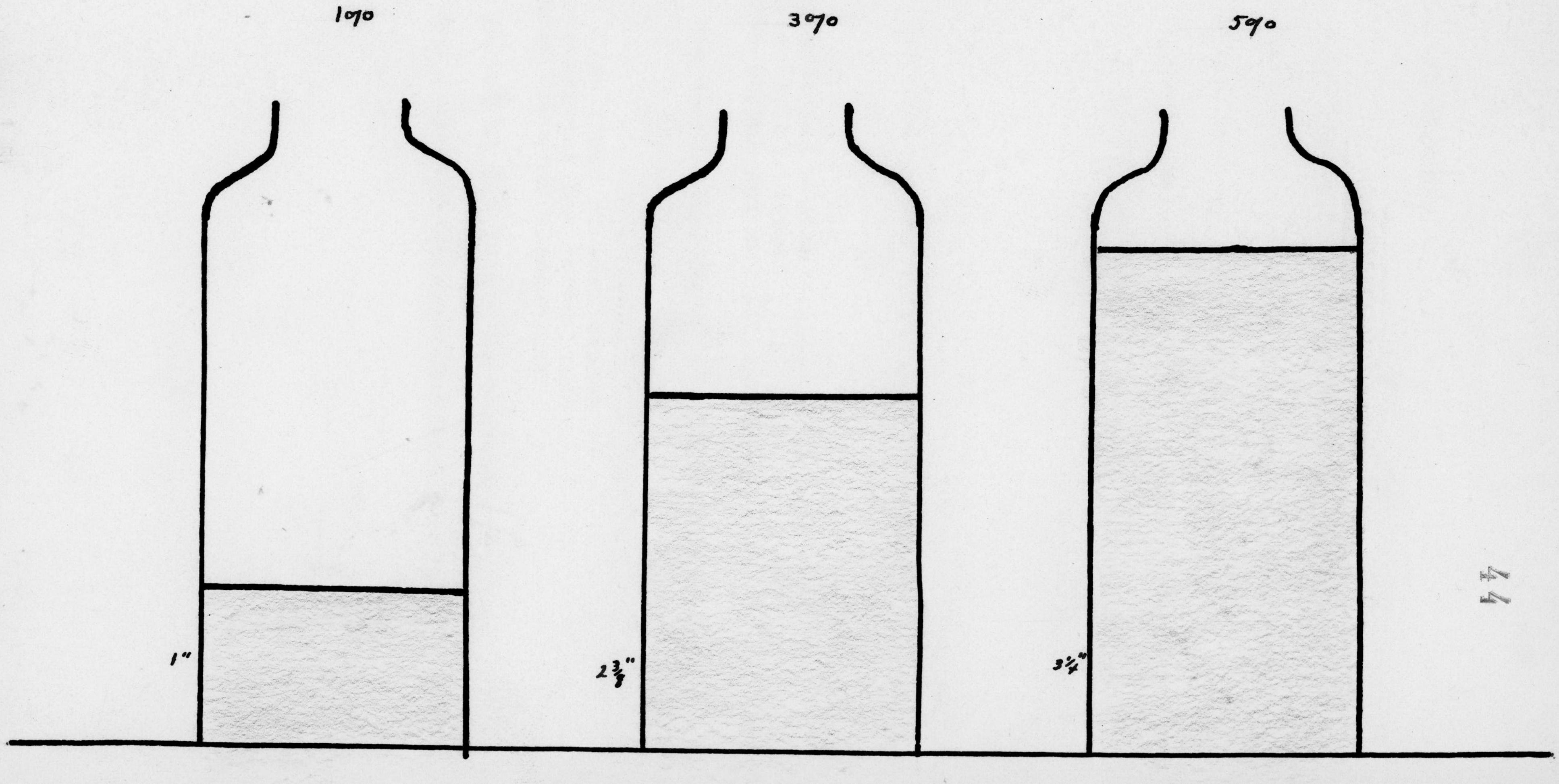
Observations under the microscope showed the following to be true:

A. 1% ..... many coalesced particles
B and C. 3% and 5% solutions ..... lumps were present in the preparation which could be seen with the naked eye, making the preparation undesirable from the dispensing standpoint.

A 1% tragacanth is the proper strength to use as a suspending agent. These observations are similar to those of Bentley.[3]

Compound Chalk Powder

Suspending Agent - Tragacanth



Bentonite

Procedure:

Stock solutions of bentonite were prepared in strengths of 1%, 3%, and 5%. Water was placed in a capacious container, usually making up about one-half the volume. To this the bentonite was added all at once and the mixture shaken vigorously. An amount of water was then added to make the solution the proper strength.

Results:

Upon standing for five hours, sedimentation occurred as follows:

A. 1% bentonite (total volume) ..... 7½/16 inch
B. 3% bentonite (total volume) ..... none
C. 5% bentonite (total volume) ..... none

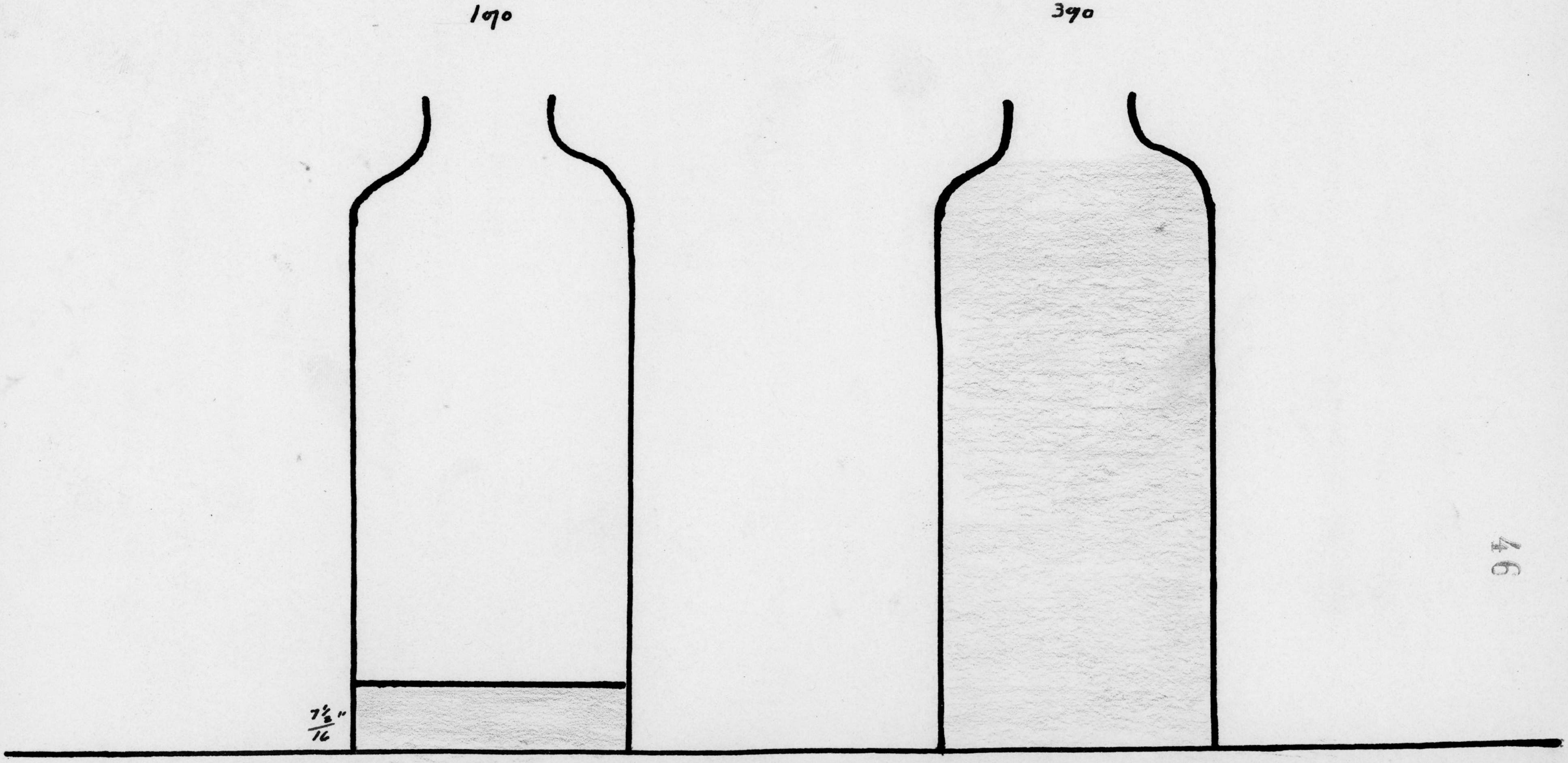
Observations under the microscope showed the following to be true:

A. 1% ..... a fine state of subdivision
B. 3% ..... coalescence has taken place
C. 5% ..... near ointment consistency

The insoluble matter in the 1% and 3% bentonite mixture was easily shaken into a uniform suspension after standing for five hours.

Compound Chalk Powder

Suspending Agent-Bentonite



Because of the fine suspending power of bentonite observed when it was used to suspend compound chalk powder, it was used to suspend the insoluble powder, prepared calamine.

Calamine lotion is official in the N.F.VI:

Prepared calamine	80 Gm.
Zinc oxide	80 Gm.
Glycerin	20 cc.
Solution of calcium hydroxide,	a sufficient quantity
To make	1000 cc.

> Mix the powders intimately with the glycerin and about 100 cc. of solution of calcium hydroxide to a smooth uniform paste. Gradually add, with agitation after each addition, sufficient of the solution of calcium hydroxide to make the product measure 1000 cc.

Procedure:

Aqueous stock solutions were used as previously explained under bentonite.

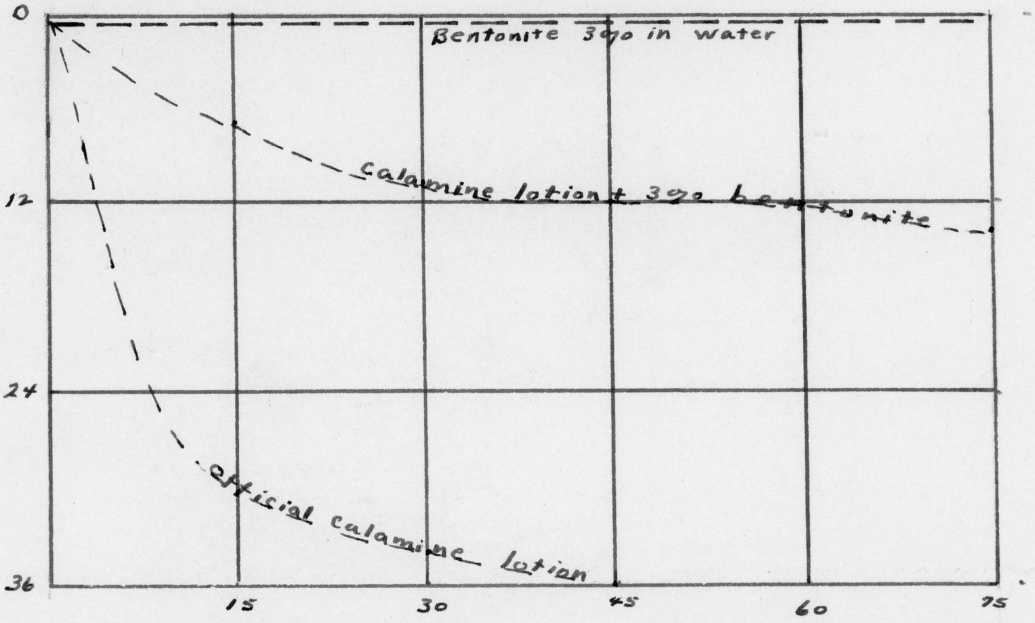
Observations under the microscope:

A. 1% ..... finely divided particles
B. 3% ..... finely divided particles
C. 5% ..... coalescence, lumping

Results:

The 1% bentonite in calamine was of little value. The 3% solution made an excellent preparation. The 5% solution, while maintaining a permanent suspension was too viscous to use as a lotion.

The following graph shows a comparison of official calamine lotion; calamine lotion plus 3% bentonite; and an aqueous 3% bentonite suspension. The vertical axis shows the sedimentation in millimeters and the time is shown on the horizontal axis in minutes.



After several days the calamine mixture containing the 3% bentonite does not settle out any more than illustrated. From the graph it is readily seen that prepared calamine when suspended in a 3% bentonite solution does not settle after an hour and fifteen minutes. The official calamine lotion settles out some after a few minutes of standing and at the end of fifteen minutes has settled out considerably. Using 3% bentonite in the calamine lotion the solution is slow in settling out and at the end of fifteen minutes has settled out approximately one-fifth as much as the calamine lotion, not containing the bentonite. At the end of thirty minutes the calamine lotion containing the bentonite has only settled out a little more than it had at the fifteen minute period.

Many mixtures of insoluble powders were prepared using bentonite as the suspending agent. The following preparations proved to be very satisfactory:

R_x

Bismuth subcarbonate	20.0
Bentonite 3% aq. sol. ad.	90.0

Procedure: Refer to bentonite.

R_x

Zinc oxide	5.0
Talc	5.0
Sodium borate	5.0
Menthol	1.4
Alcohol	15.0
Bentonite aq. sol. 3%	90.0

Procedure:

Dissolve the menthol in the alcohol, the sodium borate in water, mix the powders in a mortar and proceed with the mixing as previously described under bentonite.

R_x

Sulfur, ppt.	3.0
Spirits of camphor	5.0
Aqueous rosae fort.	15.0
Bentonite 3% aq.	q.s. ad. 60.0

Procedure: See under bentonite.

R_x

Phenyl salicylate	
Bismuth subcarbonate	
Elixir lactated pepsin	q.s.

Procedure:

Mix one dram of bentonite with the elixir of lactated pepsin and proceed as previously described under bentonite.

Results:

After two hours there is little or no separation in these mixtures. There is a fine state of subdivision and the mixtures are readily shaken into a state of suspension.

Conclusions:

1. Bentonite is a valuable suspending agent because:
    a. It prevents the insoluble powder from forming a hard mass at the bottom of the bottle. By keeping this powder in a fine state of subdivision it enables the medicament to be administered so that it will not irritate the inflammed areas to which it is applied.
    b. Because of their fineness, mixtures containing bentonite, are easily shaken into a state of suspension.
2. For a solution containing from 5% to 25% of insoluble powder, 3% bentonite is necessary to hold the powder in suspension. These suspensions do not settle out for a period of at least two hours, and upon standing one-half day, show little separation.
3. Mixtures containing acacia are somewhat difficult to shake into solution upon standing because of the formation of a cement-like mass in the bottom of the container. 3% acacia is the proper strength to use, but its suspending power does not compare with bentonite.
4. 1% tragacanth has little suspending property, but is probably the most satisfactory strength of tragacanth to use.

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