

COLLOID CHEMISTRY AND ITS APPLICATION IN PHARMACY.*

BY C. B. JORDAN.¹

When one of my friends read this title, his comment was "Well, that is some job." Since I have begun it, I agree with him. In fact, the task is so great, I cannot hope to accomplish it, but only touch upon the bare outlines of the subject. Colloid chemistry has grown so rapidly it has now become a separate branch of the general subject and courses are offered in it, just as we have courses in general chemistry, qualitative and quantitative analysis, organic chemistry, physical chemistry, etc. A laboratory manual of colloid chemistry has recently appeared. The subject is so comprehensive, I can only hope to scratch the surface. If I am able to point out part of the ramifications of colloid chemistry in pharmacy, I will be content.

Bancroft says that colloid chemistry is the chemistry of grains, drops, bubbles, filaments and films. It is the chemistry of small things, grains or small solid particles, drops or small liquid particles, bubbles or small gas particles, filaments in which all dimensions are small but one, and films in which only one dimension is small. Strictly speaking there is no such thing as colloid chemistry, because most if not all substances can be made in a sufficiently finely divided condition to be in the "colloidal state." Holmes describes this state of a substance as existing in particles between 100 millimicrons and 0.1 millimicron in diameter. (A millimicron being one-millionth of a millimeter in diameter.)

The smallest particle that can be seen by our best microscope is about 100 millimicrons in diameter. Therefore we are speaking, roughly, of substances that are between 100 millimicrons and 0.1 millimicron in diameter. If we can subdivide a substance until it falls between these limits, it is in the colloidal state. It is the mere matter of size of particles and each particle is perhaps made up of hundreds or thousands of molecules.

Colloids have some of the characteristics of true solutions. They are clear to the naked eye and to the best microscopes and they are unfilterable, but they give color and can, by the aid of the ultramicroscope, be shown to consist of minute particles. They have many characteristics that true solutions do not have, they show great adsorptive power, they often act as protectives preventing precipitation or coalescence, they can be precipitated by strong electrolytes, and they can be purified by dialysis.

Adsorption.—Holmes states that adsorption is a "surface holding" and depends largely, if not wholly, on extent of surface. If this be true, a finely divided substance or colloid will show great adsorptive power. We can better understand how subdivision increases surface by an illustration: A cube 1 cm. on edge has 6 sq. cm. of surface. If this cube be subdivided until it is 100 millimicrons on edge, the surface is 600,000 sq. cm. and the number of particles is increased to 10^{18} . We have increased the surface 100,000 times. Since adsorption is a function of surface extent, we have greatly increased the adsorptive power. Adsorption is one of the most important characteristics of colloids and advantage is taken of it in many industrial processes.

* Section on Education and Legislation, A. Ph. A., Cleveland meeting, 1922.

¹ Purdue University.

The greater part of the efficiency of gas masks depended upon the adsorptive power of the charcoal filler. Filter paper adsorbs appreciable quantities of Ba, Ca and Sr hydroxides, therefore in quantitative analysis weak standard solutions of these substances should not be filtered. Bancroft states that when $\frac{1}{2}$ grain of strychnine was added to $\frac{1}{2}$ gallon of water and this was shaken with 2 ounces of animal charcoal and filtered, the filtrate did not show a trace of strychnine even with our most delicate tests. The strychnine was recovered from the charcoal by shaking with alcohol. We have all used charcoal to remove color from organic solutions. We must bear in mind that the charcoal may remove some of the constituents we are endeavoring to secure. In the purification of alkaloids, animal charcoal has been used. Here again there is danger of losing the alkaloid. The disagreeable odor of raw whisky can be removed by leaching it through charcoal due to the adsorptive power of the charcoal.

A fine-grained sponge will hold 30 Gm. of water per Gm. of sponge, and a coarse-grained one will hold 5 or 6 Gm. of water per Gm. of sponge. Absorbent cotton could well be called adsorbent cotton, because its value rests in a great measure upon its adsorbent properties. Here we have an example of a filament colloid with all dimensions small except one. Good absorbent cotton will hold 4 grams of water when centrifuged at 4000 r. p. m. Part of the water is held in capillary spaces and part adsorbed upon the surfaces. Sphagnum moss will imbibe 200 times its own weight of water. This explains its use as a dressing in the trenches.

There has been considerable discussion regarding the mechanism of the starch-iodide combination. It was once thought to be a chemical combination, but it is more than likely that the starch adsorbs the iodine. If a weak solution of iodine is filtered through charcoal, it can be made colorless. This is a new method of preparing colorless iodine preparations. The resulting liquid will probably be as efficient as that prepared by the use of sodium thiosulphate. Phosphate baking powders are protected from moisture by starch. It is important that the calcium phosphate be not too finely ground nor the starch too coarse. Here the starch adsorbs the moisture and thus prevents reaction between the phosphate and the carbonate.

In the determination of alums, we must use care as the aluminum hydroxide has a tendency to become colloidal and adsorbs ions that may not be volatilized on heating. The precipitate should be well washed and, if possible, volatile salts should be used in precipitation. Owing to adsorption indicators are often unreliable in determining the hydrogen ion in protein solutions. We should take this into consideration when determining the acidity of albuminous urine.

Selective Adsorption.—Colloids often show selective adsorption, adsorbing some ions and not others, or some ions to a much greater extent than others. Infusorial earth is used to clean greasy glass because it has selective adsorption for the grease. Many spot cleansers owe their efficiency to selective adsorption. Holmes states that when AgNO_3 is added to a slight excess of KI a negative colloid is formed, due to the selective adsorption of the iodide ion. If, on the other hand, a slight excess of AgNO_3 is present, a positive colloid is formed, due to the adsorption of the positive Ag ion. The salt shows selective adsorption for its own ions.

Selective adsorption may cause neutral salt solutions to show basic or acidic reactions. Neutral solutions will become acidic if shaken with colloids that adsorb

bases, and alkaline if shaken with colloids that adsorb acids. Bancroft says that if fuller's earth be shaken with a solution of sodium chloride and the solution filtered, the filtrate will be acid to litmus. If you press litmus against moistened fuller's earth, it turns red. If you add fuller's earth to a slightly alkaline solution of phenolphthalein the red color disappears. The fuller's earth has in each case adsorbed the base. Advantage can be taken of this to remove a small amount of base from solution. We are all familiar with the fact that linseed oil will displace water in contact with white lead, the lead showing selective adsorption for the oil. The cleansing action of soap is due in a great measure to the selective adsorption of dirt. If the soap be alkaline it will saponify the grease, but its efficiency rests chiefly upon its adsorptive power. In hot water some soap goes into solution but most soap solutions are colloidal and hence show adsorption.

Peptization.—It is a well-known fact that pepsin changes coagulated egg-white to peptones if a trace of HCl be present. The albumin is changed to the colloidal peptones. Graham called this peptonization, but most colloidal chemists to-day call it peptization; that is, when a colloidal gel is converted into a sol or subdivided into particles far larger than molecules it is peptized. Holmes says that acacia, glue, gelatin, soap and dextrine are not dissolved in water but are peptized by the water and they are really colloidal solutions. The same is true of our collodions. They are not true solutions. The guncotton is peptized by the ether-alcohol menstruum, rendering them colloidal suspensions. Bancroft makes an observation that should be of deep interest to pharmacists. He says "It is not very easy to peptize gum arabic by grinding with water because the water does not readily displace the air from the gum. If the gum is ground a moment with alcohol, the water wets it readily. This is surprising because water peptizes the gum and alcohol does not, one would consequently have expected it to be adsorbed more strongly than the alcohol. It is possible that there is a film of grease on the gum which is removed by the alcohol. It is also possible that the alcohol displaces the air more rapidly because it absorbs air more strongly than does water." If what Bancroft says is true, it would be better to grind gum arabic with a little alcohol before adding water in making emulsions. This is worth investigating.

Peptization of precipitates by adsorbed ions is common. The colloid becomes positive or negative depending upon whether positive or negative ions are adsorbed. Clays are more easily peptized if a trace of alkali be present, due to the preferential adsorption of hydroxyl ions. Advantage of this is taken in making colloidal suspensions of clay. A suspension of clay with a trace of base, iron and organic matter can be made so fine that each particle shows Brownian movement. In a recent analysis of a fake hog cholera preparation, I found this to be true.

Protective Colloids.—It has been known for years that certain substances aid in keeping precipitates in suspension. We often use them in pharmacy to peptize precipitates and keep them in a fine suspension. The action of gelatin in protecting AgI, AgBr and AgCl is a common one and often used in pharmacy. Gelatin, casein, albumen, agar, dextrine, acacia, tragacanth and glue interfere with the precipitation of many insoluble compounds and hence act as protective colloids.

There are two or three theories advanced to explain the action of protective colloids. Some chemists believe that the colloid forms a film around the particles

and prevent them from uniting. Others believe that they are solvated colloids and "bind" the water. Others believe that the action is due to the adsorption of the protective colloid and the protected precipitate by each other. No matter what the explanation of this action, it is important that pharmacists be aware of their value in keeping precipitates in suspension.

The efficiency of the different protective colloids is of importance. Zsigmondy has determined the relative protective power of these substances and expresses it as the "gold number" of the colloids. The gold number is the number of milligrams of protective colloid which just prevents the color change in a 10-cc red-gold solution when 1 cc of a 10% NaCl solution is added. A study of Zsigmondy's table is of interest. The table follows:

Substance.	Gold No.	Reciprocal of Gold No.
Gelatin and glue	0.005-0.1	200-100
Casein	0.01-0.02	100-50
Acacia (good)	0.15-0.25	6-8
Acacia (poor)	0.5-0.4	2-2.5
Tragacanth	2	0.5
Dextrine	(6-12)	(0.17-0.08)
	(10-20)	(0.1-0.05)

If Zsigmondy's gold numbers mean anything, they are worthy of study. The table shows that gelatin is 20 times more efficient as a protective colloid than good acacia and casein is 10 times more efficient. Zsigmondy indicates that there is considerable difference in protective power of good and poor acacia, the good being 3 to 6 times as efficient as the poor. I sometimes think that pharmacists are too well satisfied with acacia in emulsion preparation. If gelatin is 20 times as efficient in protective power, why not use it? This seems to be a fertile field for investigation. Out of such research may come a better method for preparing emulsions.

Protective colloids are not very sensitive to electrolytes and salt solutions may be added to suspensions containing them without causing precipitation. Argyrol, protargol, collargol and silvol are said to be of this nature. A little gelatin added to ice cream acts as a protective preventing the formation of small ice crystals and giving a smooth velvety taste. Lactalbumin of milk has high protective value and mothers' milk contains more of it than cows' milk. Some physicians advocate the addition of a little gelatin to cows' milk in infant feeding as the curd formed is of looser texture and more easily digested.

Coagulation of Colloidal Suspensions.—Colloids are either positively or negatively charged, depending upon whether the adsorbed ion is positive or negative. Electrolytes, neutralizing the charges, cause coagulation of colloidal suspensions. All pharmacists are familiar with the difficulties experienced in adding acids, alkalis or solutions of salts to emulsions. In analysis we precipitate arsenic from a strongly acid solution to prevent colloidal As_2S_3 from being formed. We also wash $Al(OH)_3$ with a solution of ammonium nitrate to prevent it from becoming colloidal and running through the filter paper. The action of salt solution in precipitating casein in making cold creams is of this nature.

The precipitating power of ions varies with the valence of the ion of charge opposite to that of the colloid. Svedberg determined that the concentration of

K^+ , Ba^{++} and Al^{+++} required to aggregate particles of As_2S_3 to the same degree stood in the ratio of 1000 : 50 : 1; that is, with an increase of valence we get the precipitating efficiency increased many times. Hatschek has shown that $AlCl_3$ is 500 times as efficient as $NaCl$ and seven times as efficient as $CaCl_2$. This would indicate that it is less dangerous to the suspended colloid to dilute it with a solution of an electrolyte of one charge than with an electrolyte of more than one charge.

Some colloids are readily coagulated by heat. Glue, gelatin, agar, albumin and jelly-like or giving substances are not readily coagulated by a low concentration of an electrolyte but are readily coagulated by heat. The heat test for albumin in urine belongs to this class while the nitric acid test belongs to the electrolyte class. It is believed that the formation of deltas is due to the coagulation of the suspension by the electrolytes in the sea water.

Elutriation is, in a measure, a function of colloidal particles. The smaller particles settle slower because they are wetted slower and hence a separation can be made. The finely divided clay mentioned above was probably prepared in this way. The size of the particles greatly influences the time of settling. $BaSO_4$ cannot be filtered if precipitated cold, but if precipitated hot and digested larger particles are produced. The smaller particles are more soluble and they dissolve and deposit upon the larger ones. Hulett found that $CaSO_4$ (1.8 micron) was soluble 2.29 mg. per liter at 25° and the same $CaSO_4$ ground to 0.1 micron was soluble 4.5 mg. in a liter. Solubility can be increased by reducing the substance to a fine state of subdivision. Holmes says that red oxide of mercury ground in a mortar turns yellow and its solubility is increased three-fold. I have not had an opportunity to test the truth of this statement but I have found that grinding red oxide changes its color toward the yellow.

In the Fehling test for sugar in urine, we often get a change of color from yellowish green to yellow, to orange, to red, depending upon the size of the particles of Cu_2O . Holmes says that too much reducing sugar is likely to yield only the greenish discoloration. With much sugar the number of points at which the copper salt is attacked and reduced will be much larger and all the copper salt will be used up while the particles of oxide are still small and thus it gives only a greenish coloration. He recommends reduction at low or room temperature and long standing. I must confess I have never had the difficulty that Holmes speaks of except that sometimes the red precipitate is slow in forming.

Dialysis.—Graham was the first to discover that certain substances would pass through a membrane and others would not. Those that would not pass through were glue-like so he called them colloids from colla (glue). As our knowledge of these things increased we discovered that there perhaps are no true colloids but most if not all substances can be made colloidal, that is, we should speak of the colloidal state instead of speaking of colloids. From Graham's work we have learned that substances in the colloidal state will not pass through membranes and others in the molecular state will. Industrial processes for the purification of colloidal substances depend upon this fact and we use dialyses frequently. Serums are purified in this way.

Holmes says that the speed of dialysis depends upon four factors: first, nature of the membrane; second, the area of membrane in contact with the liquids on both sides; third, the difference in concentration of the diffusible substance on

both sides of the membrane; fourth, the temperature of the two liquids. The first three of these are nearly axiomatic but the fourth factor may be overlooked in speeding up dialysis.

Emulsions.—This subject needs no discussion before pharmacists except perhaps to point out the differences in protective power of colloids as before mentioned. It may be interesting to some to state that we may have two types of emulsions depending upon which substance is in the dispersed phase. We may have emulsions of oil in water in which the oil is dispersed or we may have emulsions of water in oil in which the water is in the dispersed phase. Much work has been done upon emulsions, but unfortunately for the pharmacists the workers used soaps, calcium and magnesium oleates, etc., as protectives, things that cannot be used in pharmacy. Holmes and Bancroft both believe that pharmacists are too particular, especially too minute in their directions for preparing emulsions.

One fact is of importance to us and that is that intermittent shaking is better for preparing emulsions than continuous shaking. Perhaps this explains why so many housewives are successful in making mayonnaise, that is, they shake it intermittently, doing other duties between times.

Effect of Division on Metals.—Finely divided metals show a much greater activity than do those that are not divided. Metallic mercury is not absorbed by the skin, but emulsified metallic mercury, mercury ointment, is absorbed readily. Finely divided metals act as good catalysts because of the surface expansion. They have been successfully used in the dehydrogenation processes. Reduced copper at 150° will convert borneol into camphor and geraniol into citral. The former is used as an industrial process.

Finely Divided Powders.—If we control the fineness of two powders, we can, on mixing them, cause either one to be adsorbed by the other. Bancroft has an interesting experiment as follows: 0.032 Gm. of Prussian blue was mixed with 10 Gm. of dolomite which passed a 40-mesh sieve but did not pass a 100-mesh sieve. The resulting mixture was a deep blue due to the fact that the fine blue particles were adsorbed by the larger white ones. In another experiment the same amounts of the Prussian blue and dolomite were used but they were both ground until they passed a 200-mesh sieve. The resulting mixture was practically white. Thus you see we can control the color of mixtures of this kind by controlling the fineness of the powders. A favorite preparation given by state boards in their practical examination is a powder consisting of charcoal and magnesium oxide. One of the purposes of the preparation is to determine the neatness of the applicant. Many applicants have the charcoal all over the desk, hands and even the face. If the applicants were permitted to control the fineness of these powders, they could surprise the board by getting a mixture that would be nearly white.

Practically the whole field of bio-chemistry is colloidal chemistry because the fluids of the body are colloidal suspensions. The pharmacist who is engaged in the analysis of body fluids will find an understanding of colloidal chemistry necessary. There is much work to be done in the three fields, colloidal chemistry, bio-chemistry and pharmacy, before these three sciences articulate properly. The fields are fertile ones for investigation and I hope that our share of original investigation will be done by pharmaceutically trained men.