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MAGNESIUM SULPHATE.\*

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Common salt has been used as a purgative by the ancients and it is reported that Paracelsus and his followers employed the tartrates of potassium for similar purposes. But the attention of physicians was drawn to this class of cathartics by Glauber in 1658 through his discovery of the *Sal Mirabile* commonly known as sodium sulphate.

In 1663 the Duke of Holstein paid 500 thalers for the secret of the preparation of the long famous *Sal Polychrestus* or *Tartarum vitriolatum*, probably a mixture of the neutral and the acid sulphates of potassium.

Seignette, an apothecary of Rochelle, prepared the sodium and potassium tartrate in 1672. Three years later, 1675, Grew first observed the presence of a purgative salt in the springs of Epsom and this salt was afterwards identified as magnesium sulphate by Dr. Black.<sup>1</sup>

The action of these salts was but indifferently understood for some time. The discovery of the phenomenon of osmosis<sup>2</sup> gave the first scientific explanation of the action of saline cathartics.<sup>3</sup> Liebig<sup>4</sup> simultaneously came to the same conclusion with Poisseuille, but did not publish his observations until some years later. However, the theory of Poisseuille and Liebig and many of their adherents that the endosmotic power of the saline alone determined its purgative action was disproven by the experiments of Aubert<sup>5</sup> who compared three of the most important saline cathartics and found that sodium phosphate possessed an endosmotic power of over twice that of sodium sulphate, and this in turn had an endosmotic equivalent of nearly three times that of magnesium sulphate. Accordingly one would suppose that sodium phosphate would be the strongest saline cathartic and magnesium sulphate the weakest, while the very opposite is the case.

In 1854 Colin<sup>6</sup> and later on Moreau<sup>7</sup> performed the now classical experiment of injecting saline solution into an isolated loop of intestines and demonstrated the increase in volume of the aqueous contents. Still the nature and origin of this increase was not clear.

## RELATIONS OF THE SALTS TO PERISTALSIS OF GASTRO-INTESTINAL CANAL.

McCallum<sup>8</sup> felt justified, after a series of animal experiments, to draw the conclusion that all those salts which act as purgatives when introduced into the stomach or intestine, have the same action when injected subcutaneously or intravenously.

Meltzer and Auer<sup>9</sup> proved that subcutaneous and intravenous injections of magnesium salts produce neither purgation nor intestinal peristalsis. The moderate peristalsis produced by exposing the intestines to air, by destroying the dorsal cord or by intravenous or subcutaneous injections of certain saline purgatives and the powerful peristaltic constrictions produced in all parts of the gastro-intestinal canal by intravenous injections of ergot, eserine, or barium chloride can be completely inhibited by an intravenous injection of magnesium sulphate or chloride in doses insufficient to embarrass the respiration to any serious degree.

The *post mortem* peristalsis of animals which received intravenous injections of magnesium sulphate is considerably less in evidence than that of normal animals.

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Auer<sup>10</sup> demonstrated in a series of experiments in which magnesium sulphate was injected into the jugular vein, in concentrations ranging from 1.7 to 25 percent, in amounts between 1 mil and 80 mils, that most of the rabbits showed no signs of purgation; the faeces passed during observation (2 to 4 hours) were dry and small in amounts.

Hay<sup>11</sup> summarizes his results as follows:

A saline purgative always excites more or less secretion from the alimentary canal, depending on the amount of the salt and the strength of its solution, and varying with the nature of the salt.

The excito-secretory action of the salt is probably due to the bitterness as well as to the irritant and specific properties of the salt and not to osmosis.

The low diffusibility of the salt impedes the absorption of the secreted fluid.

Between stimulated secretion on the one hand and impeded absorption on the other there is an accumulation of fluid in the canal.

The accumulated fluid, partly from ordinary dynamical laws, partly from gentle stimulation of the peristaltic movements excited by distension, reaches the rectum and produces purgation.

Purgation will not ensue if water be withheld from the diet for one or two days previous to the administration of the salt in concentrated form.

The absence of purgation is not due to the want of water in the alimentary canal but to its deficiency in the blood.

Under ordinary conditions, with an unrestricted supply of water, the maximal amount of fluid accumulated within the canal corresponds very nearly to the quantity of water required to form a 5 or 6 percent solution of the amount of salt administered.

If, therefore, a solution of this strength be given it does not increase in bulk.

If a solution of greater strength be administered it rapidly increases in volume until the maximum is attained. This it accomplishes in the case of a 20 percent solution in from one to one and a half hours.

After the maximum has been reached it begins gradually and slowly to diminish in quantity.

*Cæteris paribus*, the weaker or, in other words, the more voluminous the solution of the salt administered is, the more quickly is the maximum within the canal reached, and accordingly purgation follows with greater rapidity.

Unless the solution of the salt is more concentrated than 10 percent it excites little or no secretion in the stomach.

The salt is absorbed with extreme slowness by the stomach of the cat.

The salt excites an active secretion in the intestines, and probably for the most part in the small intestines, all portions of this viscus being capable of yielding the secretion in almost equal quantities.

The salt does not purge when injected into the blood and excites no intestinal peristalsis.

The magnesium sulphate is powerfully toxic when injected into the circulation, paralyzing first the respiration and afterward the heart and abolishing sensation or paralyzing the sensory-motor reflex centers.

According as the salt solution within the intestine increases in amount there occurs a corresponding diminution of the fluid in the blood.

The blood recoups itself in a short time by absorbing from the tissues a nearly equal quantity of their fluids.

The salt, after some hours, causes diuresis, and with it a second concentration of the blood which continues so long as diuresis is active.

Leubuscher<sup>12</sup> takes up the theory advanced by Liebig and Poisseuille that the act on of the salt is purely due to endosmosis, that of Auber with reference to cathartic action when introduced parenterally and Hay's and Voit's, Bauer's, Moreau's, Laidler Brunton's etc., all with reference to influence of the salts on peristalsis. The results of his experiments seem to show that:

The increase in peristalsis plays only a minor part in the cathartic action of the salt.

No matter how the salts are introduced into the intestines there is always a secretion of fluid into the canal, and this is to be considered the main cause of the cathartic action.

There is no evidence that the salt inhibits resorption.

When introduced into circulation in sufficient amounts these salt have a constipating effect.

The investigations of Meltzer<sup>13</sup> on the nature of the action of magnesium as a cathartic suggest that magnesium sulphate when introduced by way of the mouth combines with the sodium chloride found in the stomach and with the alkalis and carbon dioxide of the circulation, and splits up into sodium sulphate and magnesium carbonate. The sodium sulphate is absorbed into the circulation and causes intestinal peristalsis. The magnesium carbonate acts possibly within the intestines in two ways: It attracts liquid within the lumen of the intestines thus distending it and probably acts directly on the mucosa as a chemical stimulus. It is possible that magnesium sulphate, either as such, or in new formed combination, may have simultaneous actions of exciting and inhibitory nature on the functions of the animal body and thus bring about tonus, rhythm and peristalsis of the intestine with resultant evacuation.

#### NERVES AND ANAESTHESIA.

Meltzer and Auer<sup>14</sup> have shown that solutions of magnesium salts, even in strong concentrations, when applied directly to the nerve trunks of animals, never seemed to produce irritation. By applications of solutions of magnesium salts to nerve trunks the conductivity can be interrupted and a more or less complete block for afferent and efferent, or normal or artificial impulses, can be established. This can be accomplished by hypertonic, isotonic and hypotonic solutions. The more concentrated the solution the sooner the effect is established.

In general it takes more time for the magnesium solutions to cause a nerve block than for other known local or general anaesthetics. The block produced in the nerves by magnesium solutions disappears sometime after removal of the solutions; the recovery of the nerve is greatly assisted by washing with Ringer's solution.

The solutions of magnesium salts affect the cardiac fibers more readily than the efferent fibers for the oesophagus and the afferent respiratory and vasoconstrictor fibers within the vagus; also the sensory fibers within the sciatic nerve are more readily affected than the motor nerve fibers. It is believed that the difference is not due to a selective action of the magnesium solutions upon the different nerve fibers but to a difference in the irritability of the nerve endings of these nerve fibers.

In 1899 Meltzer<sup>15</sup> demonstrated, on a rabbit, that the effect of an intracerebral injection of potassium chlorate was that of producing a long series of convulsions, forced movements, opisthotonus, etc., and in another rabbit the opposite effect by intracerebral injection of magnesium sulphate. Without preceding convulsions the rabbit became paralyzed in a short time. No explanation of this phenomenon was made at that time. In subsequent experiments made by Meltzer and Auer<sup>16</sup> it was determined that:

A certain dose of magnesium sulphate will produce a deep, often long-lasting anaesthesia with complete relaxation of all the voluntary muscles and aboli-

tion of some of the less important reflex activities, which anaesthesia terminates in complete recovery.

That a large dose of magnesium salts will produce a profound anaesthesia and general paralysis which sooner or later leads to a calm death without being preceded or accompanied by any symptoms of excitation . . . . and not a single instance was observed in which that salt produced an increase of excitation; on the contrary any effect which this salt produced was invariably in the direction of a reduction of excitation or of its complete temporary or permanent abolition.

Haubald and Meltzer<sup>17</sup> were the first to report the production of spinal anaesthesia by magnesium sulphate.

Emil Stransky<sup>18</sup> has established the fact that subcutaneous injections of magnesium sulphate which produce narcosis cause an increase of the magnesium salts in the blood plasma; in the other organs there is either no increase at all or but very slight increase in the magnesium contents.

The relation of calcium contents to magnesium contents in the serum, which normally is strongly on the calcium side, is considerably altered in favor of magnesium so that the magnesium contents exceed even after awakening. It appears that the condition of narcosis is determined by a definite maximal value of the Ca/Mg quotient.

#### TETANUS.

Meltzer and Auer<sup>19</sup> show that: Intraspinal injections of magnesium sulphate, in doses which do not affect the respiratory center or other vital function, are capable of abolishing completely all clonic convulsions and tonic contractions in cases of human tetanus, and experimental tetanus in monkeys. The relating effects of the injections may last 24 hours or longer. In experimental tetanus in monkeys early intraspinal injections of magnesium sulphate are capable of retarding the progress and development of the tetanic symptoms.

The usual amount used in humans is 1 Cc. of a 25 percent solution for every 20 pounds of body weight.

A number of cases of successful treatment of tetanus by means of magnesium sulphate administered intraspinaly are to be found in the medical literature<sup>20-23</sup>.

On the other hand there are a number of cases, similarly treated, with fatal termination<sup>29-32</sup>:

Rozenowsky<sup>33</sup> reports from observations made during the present war that whenever the antitoxin treatment was associated with magnesium sulphate injections, either intralumbar or subcutaneous, the most favorable results were obtained. Furthermore he asserts that no unfavorable results or dangers from the use of magnesium sulphate were observed by them.

Robertson<sup>34</sup> gives a summary of some results obtained by the different methods of administering magnesium sulphate in tetanus.

*Intraspinal Method:* (4-5 Cc. of 25 percent solution) 81 patients, severe cases, with incubation period of less than five days, 36 died, 45 recovered, mortality 44.4 percent.

Anders and Morgan: 216 cases.

|                                    |  |
|------------------------------------|--|
| 38 cases incubation period 5       | days or less, no antitoxin—mortality 95%   |
| 23 cases incubation period 5       | days or less, plus antitoxin—mortality 74% |
| 58 cases incubation period 6-10    | days or less, no antitoxin—mortality 79%   |
| 56 cases incubation period 6-10    | days or less, plus antitoxin—mortality 71% |
| 18 cases incubation period over 10 | days no antitoxin—mortality 93%            |
| 23 cases incubation period over 10 | days plus antitoxin—mortality 35%          |

Robertson concludes that . . . . the administration of magnesium sulphate by intralumbar injection has brought about a definitely certain, even if small, decrease in the percentage of deaths from tetanus, as well as causing an undoubted diminution in the agony and suffering etc., etc.

*Subcutaneous Method:* (0.57 Mg. per kilo). Twelve cases, incubation period 6–10 days, mortality 8.3 as compared with 48.6 percent for the same group treated by intralumbar method. In addition to this 15 cases with incubation period of 10 days and over all recovered, reducing the mortality rate quoted above to 3.7 percent.

*Intravenous Method:* (3 percent solution). No conclusive data. Dangers: Overdose rapidly injected into vein; instant death; heart stops before respiration; such accidents rarely happen with subcutaneous injections. The sudden untoward action of the magnesium salts can be overcome by injections of calcium chloride,<sup>35</sup> or by physostigmine.<sup>36</sup>

We may conclude our remarks on magnesium sulphate and tetanus with a reference to Meltzer,<sup>37</sup> who points out that the fatal issue in tetanus is principally due to the spasms which profoundly affect the functions of respiration and circulation. He synthesizes briefly the four ways of magnesium sulphate medication in tetanus as follows:

1. *Subcutaneous injections.*—Dose not to exceed 2 Cc. nor less than 1.22 of the 25 percent solution per Kg. body weight. To be injected four times in 24 hours. No massage. Light etherization or morphinization should precede the injection of magnesium sulphate.

Administered in this way magnesium sulphate exerts its effect very slowly and principally by cumulative action. Will not relieve immediately severe and dangerous spasms.

2. *Intramuscular injections and inhalation of ether.*—The patient should be fairly well etherized and 2 Cc. of a 25 percent solution magnesium sulphate per Kg. body weight be injected into the muscles of the thigh. At the end of the injection massage the thigh and continue light ether anaesthesia for about 20 minutes longer. This method may greatly relieve even severe spasms, in less than half an hour, but the beneficial effect is liable to pass off completely after two or three hours. There may be local reaction and for this reason the injections should not be repeated too often nor should this method be used as a routine treatment.

3. *Intravenous injections.*—The concentration of the solution should be about 3 percent (isotonic) and not more than 5 Cc. per minute should be permitted to run into the vein. This mode of administration is capable of relieving dangerous effects of the spasms (tetanus of the diaphragm, constriction of the larynx) more promptly than any other method of application. But the beneficial effect may completely disappear in less than 30 minutes and furthermore the circulation may become affected by direct action on the myocardium. This method should therefore be reserved for emergency cases only.

4. *Intraspinal Injection.*—The dose to be injected, at the usual place in the lumbar region, should be 1 Cc. of a 25 percent solution for every 10 Kg. of body weight. The results of this method of treatment may become evident in less than half an hour, and after one hour the relaxation may be complete. The extent as well as the duration of the relief afforded to the patient is greater when the magnesium solution is given by the intraspinal method than by any other method of administration. The relief may last between 12 and 30 hours.

#### SEPSIS.

Harrar<sup>38</sup> used a solution of 30 grains magnesium sulphate in 8 ounces of water, and sometimes a similar quantity of a 2 percent solution for intravenous injections in a number of cases of puerperal sepsis. In all of his cases blood culture and uterine culture were made, many proving positive, showing streptococci. The remarkable results obtained lead the author to the conclusions that:—In the quantities and

dilutions described it is absolutely harmless when administered intravenously to women suffering with puerperal infection. That it is of more value early in the course of infection and seems to be of no value in chronic cases of secondary thrombophlebitis or pyemia. That the action of the drug seems to be chiefly on the organisms circulating in the blood. That it shortens the course of bacterial toxemias; and that it has reduced the mortality in puerperal septicemia in their hospital, from 93 to 20 percent.

According to Huggins,<sup>39</sup> a number of cases suffering from puerperal infection were treated by *slow* intravenous injections of magnesium sulphate with remarkably favorable results.

Freese<sup>40</sup> reports the use of magnesium sulphate and glycerin in the treatment of infections. A number of cases of infections (external) yielded very promptly to "hot solution of glycerin and salt" but he does not state the proportions used.

#### ACTION OF MAGNESIUM SULPHATE ON HEART, ETC.

Mathews and Jackson<sup>41</sup> hold that the action of magnesium sulphate upon the heart is practically the same throughout the mammalian, avian, reptilian and amphibian classes. This action consists of a very marked depression, characterized by an immediate decrease in the amplitude of the heart beat and of simultaneous progressive slowing which soon leads to a complete standstill, from which the heart may be recovered by artificial stimulation. Adrenalin and squill can not be used to offset this depression.

MacNider and Mathews,<sup>42</sup> after a discussion of the various theories as to origin and maintenance of the heart beat, and based on their observation of the behavior of the heart in response to certain physical and chemical stimuli while under the influence of magnesium sulphate, conclude that magnesium sulphate depresses the nervous mechanism in the heart, both accelerator and inhibitory—the latter more than the former to such an extent that it will not transmit to the contractile tissue impulses of the same degree as are set in by the usual physiological stimulus, whatever that may be, but that it will transmit the stronger electrical stimulus or the normal motor impulse after the heart muscle has been rendered more irritable.

#### RESPIRATION.

Meltzer and Auer<sup>43</sup> proved that magnesium salts in intravenous injections are very toxic, even in small doses, and that repetition of the injections within a relatively short time increases the susceptibility of the animal to the toxic effect. The first effect is on the respiration, which becomes completely inhibited. The respiratory center is deprived of its responsiveness to asphyxiated blood, and the reflex effect of sensory stimuli is greatly reduced. Large doses of salt, injected with rapid speed, affect also the tonus of the vasomotor center, but this toxic effect is not, as a rule, extreme and wears off sooner than the effect on the respiratory center.

#### SALIVARY DIGESTION.

Patten and Stiles<sup>44</sup> have shown that even concentrated solutions of magnesium sulphate do not inhibit the action of ptyalin on carbohydrates. The most striking instances of accelerating effects (upon the action of ptyalin) were obtained with salts of magnesium, calcium and barium.

## ANTAGONISTIC ACTION OF CALCIUM AND MAGNESIUM SULPHATE.

Meltzer and Auer<sup>45</sup> show that apparently the respiratory mechanism, which becomes affected by magnesium more readily than any other function, is also more easily protected against this influence by calcium. Intravenous infusion of various calcium salts is capable of completely reversing the pronounced inhibitory effects brought on by various magnesium salts. The respiratory paralysis, the lost lid reflex, the motor paralysis, the lost general reflexes, the general anaesthesia, the loss of consciousness, the depression of the cardio-inhibitory action of the vagus, the lowering of the blood pressure—all are reversed and completely restored in a very short time by the injection of a comparatively small quantity of calcium salt. This does not hold good, however, for conditions brought about by large doses of magnesium.

On the other hand strontium differs in its action from that of calcium with respect to the neutralization of the inhibitory effect of magnesium. While it (strontium) does cause a very slight improvement of the respiration it seems to aggravate and hasten the inhibitory symptoms due to magnesium, especially the paralysis.

Joseph<sup>46</sup> has demonstrated that eserine tremor can be abolished by magnesium sulphate and that magnesium has a certain value as antidote for eserine poisoning but not on eserine myosis.

Joseph and Meltzer<sup>47</sup> also gave a demonstration on rabbits before the American Physiological Society: One rabbit received an intramuscular injection of 1.2 Cc. magnesium sulphate per kilo body weight with fatal results. Another rabbit received a similar dose of magnesium sulphate with a simultaneous injection of barium chloride and this rabbit appeared to be in good, normal condition, while still another rabbit, receiving a dose of barium chloride similar to that given to rabbit No. 2, promptly succumbed. The authors draw these conclusions from their work: The fatal action of magnesium is due to paralysis of respiration and barium counteracts just this effect of magnesium. It differs from the antagonistic action of calcium inasmuch as calcium antagonizes all the effects of magnesium while barium picks out only the respiration, the animal remaining anaesthetized, and paralyzed. Furthermore the experiment also proves that magnesium antagonizes the fatal effect of barium.

## PATHS OF EXCRETION.

Mendel and Benedict<sup>48</sup> show that when soluble magnesium compounds are introduced parenterally into animals the greater portion of the excess injected leaves the body by way of the kidneys in less than 48 hours, thus emphasizing the importance of the kidney in the elimination of magnesium salts. The intestinal path is of minor, if any, significance for magnesium introduced under these conditions. A considerable quantity of magnesium may be retained in the body for a period of two weeks. The parenteral introduction of magnesium sulphate in dogs and rabbits is never followed by purgation.

The increased excretion of magnesium by the kidneys is accompanied by a marked rise in the urinary output of calcium while the calcium output in the faeces is decreased at the same time.

Inasmuch as magnesium sulphate was much in use for various purposes, among these the administration, subcutaneously, to relieve tetany in children, Courtney

and Fales<sup>49</sup> undertook a series of experiments to ascertain the rate of elimination in order to avoid a possible toxic accumulation of the salt in the body. They come to the conclusion that magnesium is eliminated rapidly enough, chiefly by way of the urine, to nullify a possible danger of cumulative effect of magnesium.

Meltzer and Lucas<sup>50</sup> show that magnesium salts when introduced subcutaneously are eliminated to a great extent through the kidneys. In nephrectomized rabbits the susceptibility to the toxic effect of magnesium salts is increased by about 50 percent.

The profound anaesthesia which a toxic dose of magnesium produces in nephrectomized rabbits may be continuous for 24 hours or longer. The cumulative effect of magnesium salts in nephrectomized rabbits is very striking. The effect of several subminimum doses is equal to the effect produced by the sum of these doses given in a single injection.

A dose which when given soon after nephrectomy is fatal, causes only a non-fatal anaesthesia when given 18 hours or later after nephrectomy. Probably at that period vicarious paths develop sufficient for the elimination of a fraction of the salts. It is probably for this reason that the profound anaesthesia produced by a proper dose of magnesium salts is partially recovered from in about 12 to 18 hours after nephrectomy.

#### BLOOD PRESSURE AND EDEMA.

Very little, if any, attention has been paid to the influence of magnesium sulphate on blood pressure.

I wish to report briefly on a few cases which have come under my personal observation.

Case 1—Woman 68 years of age. Paroxysmal tachycardia. B. P. 185 mm. Hg. Systolic; 110 diastolic. A daily dose of 4 Gm. magnesium sulphate in 25 percent dilution (16 Cc. oral administration) resulted in a reduction of the systolic pressure to 154, diastolic 104, with marked prolongation of tachycardial intervals.

Case 2—Man 70 years of age, marked dyspnoea, irregular arrhythmia, cardio-nephritic. Systolic 180, diastolic 100. After six months' treatment there has been a gradual drop in the systolic pressure to a final 146 with unchanged diastolic and marked improvement in breathing. It has remained *status quo* for the past four months with only an occasional dose of magnesium sulphate.

Case 3—Woman 72 years of age. Edema of extremities, nephritic and diabetic. Mitral and aortic lesions. Systolic 240, diastolic 160. Has been under treatment for two and a half years. Daily dose of 4 Gm. magnesium sulphate. At present 165-110. Urine shows only an occasional trace of albumin. Glycosuria is intermittent, no edema.

Several other cases have shown similar results but those quoted are the most striking in the series. The action of the magnesium sulphate in these cases is two-fold: First, by its purgative action it prevents intestinal stasis and reduces the resulting auto-intoxication to a minimum; second, by adsorption of water from the blood and tissues it reduces the circulating volume and decreases the blood pressure and edema. It must be borne in mind that the magnesium sulphate should be administered in concentrated form and no water must be allowed within three hours after administration of the drug.

#### PALATABLE MIXTURES.

In conclusion I wish to mention a few ways in which magnesium sulphate may be administered in a palatable way. For the sake of simplicity I have presented these in the form of prescriptions:—



1. Magnesium Sulphate..... 30.00 Gm.  
Aromatic Sulphuric Acid..... 8.00 mils  
Water..... 60.00 mils  
Glycerin to make..... 120.00 mils  
Dose: One tablespoonful.
2. Magnesium Sulphate..... 30.00 Gm.  
Fresh Orange Juice..... 30.00 mils  
Water..... 60.00 mils  
Glycerin to make..... 120.00 mils  
Dose: One teaspoonful.
3. Magnesium Sulphate..... 30.00 Gm.  
Tincture Cardamom Comp... 10.00 mils  
Citric Acid..... 1.00 Gm.  
Water..... 60.00 mils  
Glycerin to make..... 120.00 mils  
Dose: One teaspoonful.
4. Magnesium Sulphate..... 30.00 Gm.  
Citric Acid..... 1.00 Gm.  
Syrup Sarsaparilla Comp... 60.00 mils  
Water to make..... 120.00 mils  
Dose: One teaspoonful.

Carlton<sup>51</sup> suggests the following mode of prescribing magnesium sulphate:

|                                 |              |
|---------------------------------|--------------|
| Magnesium Sulphate.....         | 1000.00 Gm.  |
| Fluidextract Cardamom Comp..    | 30.00 mils   |
| Vanillin.....                   | 1.50 Gm.     |
| Garantose.....                  | 16.00 Gm.    |
| Alcohol.....                    | 16.00 mils   |
| Glycerin.....                   | 60.00 mils   |
| Coffee (roasted and ground).... | 60.00 Gm.    |
| Water to make.....              | 2000.00 mils |

DIRECTIONS: Stir the ground coffee in 2000 mils of boiling water, let stand 10 to 20 minutes. While hot add the magnesium sulphate and stir until dissolved. Dissolve the vanillin in the alcohol, add the glycerin and fluidextract and mix with the magnesium sulphate solution; when cold add the garantose, filter and bring up to the volume by addition of water. Thirty mils contain 15 grammes of magnesium sulphate.

#### SUMMARY.

- 1.—Magnesium sulphate is one of the promptest acting saline laxatives of our present materia medica.
- 2.—The degree of dilution modifies the rapidity of action.
- 3.—The mode of its cathartic action is presumably due to a combination of absorption of fluid from the blood, stimulation of secretion by the intestinal mucosa and increasing tonus and stimulating peristalsis of the intestinal musculature.
- 4.—Subcutaneous and intravenous injections do not produce catharsis.
- 5.—It produces local and general anaesthesia, but is not free from danger by reason of its marked depression of the respiratory center.
- 6.—Its toxicity is in inverse proportion to the ability of the animal to eliminate it from the system.
- 7.—Elimination takes place chiefly by kidney.
- 8.—The toxic effects are antagonized by calcium, barium and strontium salts but each to a different extent.
- 9.—It has proven of value in septic conditions, both local and general.
- 10.—In the treatment of tetanus, particularly in association with antitoxin, it has robbed war of some of its terrors.
- 11.—In concentrated solution it reduces blood pressure and edema.
- 12.—A few methods for dispensing palatable magnesium sulphate for oral administration are suggested.

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### SOY BEANS AND SOY BEAN OIL.\*

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This bean is a native of southeastern Asia. It is at present the most important legume grown in Japan, China and Manchuria, where it is grown almost exclusively for human food. It has been cultivated from a remote period, each district having its own distinctive variety, some two hundred kinds in all. It was brought to Europe in comparatively recent times and there cultivated in botanic gardens for more than a hundred years without attracting any particular attention. The bean was introduced into England in 1790. Apparently the first mention of soy beans in American literature, was in the *New England Farmer*, October 23, 1829, in an article by Thomas Nuttall. He grew a variety with red flowers and chocolate-

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