PRACTICAL PHARMACY SECTION

EMERGENCY SUBSTITUTES FOR SUGAR, SYRUP AND GLYCERIN.*

BY CURT P. WIMMER.

In bringing the subject of emergency substitutes for sugar, syrup and glycerin before you at this time, I hope that no one will take from this paper the impression that I advocate the illegitimate use of substitutes in any manner, shape or form. The word "substitute" has an unpleasant flavor in American pharmacy and the "substitutor" in normal or abnormal times is an unprincipled scoundrel who fully deserves whatever punishment the law provides for him.

Neither do I desire to appear before you as an alarmist who proclaims that sugar and glycerin will shortly disappear from the market or that their use for medicinal purposes will be prohibited by the government. On the contrary, I have entire confidence that our government will at all times see to it that a moderate supply will be available for medicinal uses.

This paper is written with only *one* object in view, and it is the following: Our country is engaged in a great war, in a war which requires that all of our resources be mobilized and strained and used for the successful prosecution of the conflict. It is the first duty of every good and loyal citizen to support the government, heed its warnings and to coöperate to the best of his ability. We are at present in the midst of a scarcity of sugar. The government has asked us to use as little of it as possible, so as to insure at least a moderate supply wherever it is needed most urgently. Glycerin also is becoming more and more scarce, a fact evidenced by the slow but steady increase in price for this substance. What, then, can the pharmacist do to assist the government? Can he get along with less sugar and glycerin in his preparations? Can he do without them altogether? What substances or preparations might possibly be used to advantage in their places?

It is the object of this paper to answer these questions. For purposes of simplicity, the paper is sub-divided into two parts, *viz.*, (1) Sugar and Syrup Emergency Substitutes, and (2) Glycerin Emergency Substitutes, and under each heading will be included a brief review of relevant conditions and means of meeting them, as found in some of the other warring countries. Most of the information regarding the latter has been gained by a careful perusal of recent foreign publications, especially of *The Chemist and Druggist* of London.

Another fundamental question must be answered: Are the quantities of sugar and glycerin used in compounding medicines so large, that their continued unrestricted use for this purpose might become embarrassing to the food administrators? Without hesitation I say "Yes." To my regret, I have no statistics available giving the amount of sugar or of glycerin used by the pharmaceutical profession

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and the drug trade, but no doubt it is very large. And furthermore, much of it, I believe, can be saved to be used either to feed the mouths of the hungry, or to be made into explosives.

About three months ago, the General Council of Medical Education of England have, by authority vested in them, altered and amended the British Pharmacopoeia and have withdrawn seventy-three preparations, with only one object in view: to save sugar and glycerin. The following preparations have been made unofficial:

(1) All Confections (except pepper and rose)

(2) All Glycerites

(3) All Mixtures (except chalk, compound iron and castor oil mixtures)

(4) All Syrups (except syrupus, chloral, codeine phosphate, iron iodide, iron phosphate with quinine and strychnine, glucose)

(5) All Troches (except krameria, cocaine, morphine, morphine and ipecac)

Also: Effervescent Citrated Caffein
Compound Decoction of Aloes
Saccharated Solution of Lime
Honey and Borax
Compound Almond Powder
Compound Licorice Powder
Suppositories of Glycerin
Compound Tincture of Cardamom
Tincture of Kino
Tincture of Wild Cherry
Comp. Tincture of Rhubarb
Comp. Tincture of Senna
Ointment of Iodine.

Surely this momentous action would not have been taken, had not actual experience shown its advisability. We may well take a lesson from countries who have been in the war longer than we have been. The withdrawal of these preparations has opened up a number of interesting questions. One of them was to the effect that, legally, this withdrawal made automatically official the older formulas which had been superseded by those withdrawn. Another point raised was that all of these important preparations were, by this withdrawal, left without any standard of any kind, a prey for the unscrupulous. The Council recently announced that they would publish substitute formulas to be used in place of the official ones, and a pamphlet regarding them is probably in the hands of the English pharmacists by this time.

The English pharmacist does, of course, not dispense any of these preparations without affixing to the container a label, showing the words "War Emergency Formula," followed by a statement to the effect that although the formula of the preparation has been changed, its physiological activity has in no wise been altered. At the same time, physicians are being requested to cease prescribing the deleted galenicals.

In our own Pharmacopoeia, sugar and glycerin are made use of in many preparations. They are, in part, the following:

Compound Licorice Powder contains		50% sugar
Compound Chalk Powder contains		50% sugar
Aromatic Elixir		31.8% sugar
Saccharated Ferrous Carbonate		70% sugar
Aromatic Fluidextract Cascara Sagrada contains		20% volume glycern
Glycerites:	Tannic Acid	80% weight glycerin
	Starch	80% weight glycerin
	Boroglycerin	69% weight glycerin
	Hydrastis	50% volume glycerin
	Phenol	80% volume glycerin
Solution Magnesium Citrate		14.5% w/v sugar
Mass of Ferrous Carbonate		25% sugar
Mucilage of Tragacanth		18% weight glycerin
Suppositories of Glycerin about		85% weight glycerin
Syrups:	Acacia	80% sugar
	Citric Acid	70% sugar
	Hydriodic Acid	57.50 volume syrup
	Orange	82% w/v sugar
	Orange Flower	85% w/v sugar
	Calcium Lactophosphate	65% w/v sugar
	Ferrous Iodide	57.5% weight sugar
	Hypophosphites	60% w/v sugar
	Ipecac	70% w/v sugar + 10% volume glycerin
	Lactucarium about	65% w/v syrup + 20% volume glycerin
	Tar	85% w/v sugar
	Wild Cherry	80% w/v sugar
	Rhubarb	85% volume syrup
	Rhubarb Aromatic	85% volume syrup
	Sarsaparilla Compound	75% volume syrup
	Squill	80% w/v sugar
	Squill Compound	83% volume syrup
	Senega	80% volume syrup
	Senna	75% volume syrup
	Tolu	82% w/v sugar
	Ginger	82% w/v sugar
Tinctures:	Gentian Compound	10% volume glycerin
	Lactucarium	25% volume glycerin
	Rhubarb	10% volume glycerin
	Rhubarb Aromatic	10% volume glycerin
Troches:	Acid Tannic	80% sugar
	Ammonium Chloride	50% sugar
	Potassium Chlorate	80% sugar
	Sodium Bicarbonate	65% sugar
Ointments:	Acid Tannic	20% weight glycerin
	Iodine	12% weight glycerin

This list is not given for the purpose of recommending the deletion of some of the formulae for the period of the war, although some such step may yet have to be taken, if the present scarcity of sugar continues, or if the supply of glycerin be withdrawn from the open market. But the list shows to what extent sugar and glycerin are used in galenical pharmacy. Add to this the amount of sugar used in the numberless proprietary remedies and you will have an idea of the total used for medicinal purposes.

In discussing various substitutes, let us not forget that they cannot be reasonably expected to be the equal in all respects of the substance they are to replace.

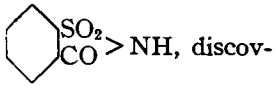
Sugar and glycerin owe their general use to the fact that they each have a number of valuable and divers properties, which make them so useful to us. A substitute for sugar, for example, cannot be expected to have *all* of the physical and chemical properties of sugar. If, however, we succeed in devising a preparation which, in a *given galenical*, will satisfactorily replace the sugar, then the substitute must be called a success. So, for different classes of galenicals, or even for certain individual preparations, different substitutes may have to be used. The nature of the substitute will depend entirely, in each case, upon the especial property of the sugar or glycerin which we desire to impart.

In England, the wholesale manufacturing as well as the retail pharmacist must make application to the local food controller for a sugar supply for the coming year. This application must be made on special blanks, which require the following information: 1—Class of manufacture. 2—Stock of sugar on hand. 3—Amount of sugar used in 1915. 4—Quantity applied for. 5—Usual supplies. 6—Remarks.

At this writing the food controller had allowed to manufacturing pharmacists 50 per cent of the total amount used by them in 1915.

1. SUGAR AND SYRUP EMERGENCY SUBSTITUTES.

In arranging the various properties of sugar according to their relative importance, in medicinal preparations, I should unhesitatingly say that, first, sugar is used because of its taste, second, because it preserves, third, because it imparts consistence or bulk, and, lastly, because it has a slight physiologic action. For purposes of substitution the last-named property must at once be discounted, since the sugar of a preparation depending in its physiological action solely upon this substance simply cannot be replaced by anything else. Such "medicines" I will exclude from consideration here. To impart to preparations a sweet taste, nothing is more suitable than saccharin.

Saccharin, or O-sulphamino benzoic acid anhydride,  , discovered accidentally by Fahlberg in 1878, is a microcrystalline powder, soluble in water 1 : 290, melts at 220° C. It is about 500 times sweeter than sugar, and, therefore, at least as cheap as sugar if it can be bought for about $40 a pound. The price of saccharin to-day is quite unsettled, but the amount of the substance that might be used in medicinals would be so small that the matter of cost would hardly play an important part. I believe that saccharin will come into its own through this war. In spite of the reports of eminent authorities that saccharin is harmless if taken in small quantity, this substance has become almost an outlaw in many countries. No doubt, economic and political considerations had something to do with the making of the laws against its use, but such considerations do not hold now and the question of a limited use of this substance in galenicals might well be discussed. Professor Joachimoglu, of the University of Berlin, is reported to have recently stated that after extensive experiments and observations during this war, he is convinced that saccharin is harmless. Professor E. R. Watson, of the University of Leeds, recommends its use in solution. In the city of Manchester, signs in various shops advertise saccharin as being "better and cheaper" than sugar. The Italian government permits the sale of an artificial sugar, a dilution

of saccharin 6 to dextrose 1000, in the pharmacies. Unfortunately, a vicious rumor has been spread in certain Italian localities among the ignorant, that this artificial sugar may cause cancer, and so the pharmacists are having a hard time trying to dispose of it.

Very recently, the *Société de Thérapeutique* of France passed resolutions requesting the government to permit the use of a saccharin-dextrose mixture, 1 : 1000, for sweetening purposes. It is, however, not be used in jams, chocolates and other articles of food.

I might also direct your attention to the report on saccharin of the Referee Board of the American Medical Association. This report shows that saccharin in small quantities, 0.3 Gm. per day or less, is without deleterious or poisonous action, that in larger quantities, especially over 1 Gm. per day, when taken for a considerable period of time, it is liable to produce disturbances of digestion. Again I ask that my position in this matter be not misunderstood. I believe that under no circumstances should the use of saccharin be permitted in any preparation which depends for its use entirely or in part, upon the presence of sugar, especially in those used as a food.

The property of syrup of lending consistency and, in more limited degrees, of preserving, may well be imparted to galenicals by glucose, or similar substances, such as honey, invert sugar, manna or molasses, or mixtures of these. The proposition most frequently met with in English current publications is to take glucose, dilute it with water to the specific gravity of syrup, 1.313, then to boil and strain and to add some chloroform. This preparation is claimed to keep for months.

Acting upon this suggestion, I procured some liquid glucose and diluted it to the desired specific gravity, but found that the viscosity of this preparation was very much higher than that of the U. S. P. syrup. Inasmuch as the specific gravity seemed to me a less desirable standard to use than viscosity, I prepared several mixtures of glucose and water and by the aid of Engler's viscosimeter established that a mixture of $66^2/_3$ percent by volume of glucose with water at 25° C. has approximately the same viscosity, or fluidity, as the official syrup. Next, I procured some Karo syrup (Crystal White brand) of the Corn Products Manufacturing Company, and established by a series of experiments that a mixture of 75 percent of this Karo with 25 percent (by volume) of water, at 25° C. has a viscosity practically the same as that of official syrup. With the kind assistance of some of our students, a series of taste experiments was carried out, with a view of establishing the relative sweetness of the various syrups. Dilutions ranging from 1 : 10 up to 1 : 200 were prepared and the concentration at which the sweet taste was first tasted distinctly, was determined. We found the following ratio:

Syrup, U. S. P., taste appears in dilution 1 : 110.

Glucose, $66^2/_3$ percent volume, taste appears in dilution 1 : 25.

Karo, 75 percent volume, taste appears in dilution 1 : 35.

Taking the sweetness of official syrup as one, it appeared that the glucose preparation was 0.227 and the Karo preparation 0.32 as sweet.

Glucose is rated to be about one-third as sweet as sugar, and basing upon this ratio, and, furthermore, upon the ratio 1 : 500 for relative sugar-saccharin sweetness, I expected that about 1.20 Gm. of saccharin would have to be added to every 1000 mils of glucose syrup to get the same relative sweetness as that of official syrup. We found, however, that sweetness cannot, with safety, be calculated by a rule of

mixtures. On making dilutions and tasting them, we found that 1.35 Gm. of saccharin are required to every 1000 mils to approximately impart the same degree of sweetness to the glucose syrup as the sucrose syrup possesses. Similar experiments made with the Karo syrup showed that 1.20 Gm. of saccharin are required for every 1000 mils of 75 percent volume syrup. The formulae read, consequently, as follows:

WAR EMERGENCY FORMULA I.		WAR EMERGENCY FORMULA II.	
Glucose, liq.....	667 mils	Karo, crystal white.....	750 mils
Water.....	333 mils	Water.....	250 mils
Saccharin.....	1.35 Gm.	Saccharin.....	1.20 Gm.

The saccharin dissolves readily upon applying heat to the syrup.

Such a preparation would, no doubt, answer very well in a number of medicinal preparations in place of syrup. It might have to be modified to suit especial cases, but that could easily be accomplished. Let us, however, not forget to mention possible objections to the use of this syrup. Liquid glucose usually contains traces of sulphur dioxide, about 200–300 parts per million. A glucose syrup cannot be used with any substance easily susceptible to reduction, and finally a glucose syrup is not as permanent as a sucrose syrup. The tendency to fermentation may, however, be overcome by an addition of a small amount of chloroform.

On the other hand, a glucose syrup might be even more advantageously used in cases where a reducing substance tends to retard decomposition as in ferrous preparations or hypophosphites. I have prepared a number of galenicals, which I submit to your kind judgment. They are syrup of hydriodic acid, syrup of ferrous iodide, syrup of rhubarb and syrup of tolu, also compound licorice powder. In the latter preparation the sugar has been replaced by a mixture of saccharin 1.50 to pure white dextrose 1000 parts. English pharmacists recommend the use of a mixture of almond meal 8 parts, and acacia 1 part, or of starch, or of a corn-meal-saccharin mixture in this case. I find the dextrose-saccharin mixture to be the best. Another substance, which, of late, has come into somewhat extensive use in place of sucrose in ice cream is invert sugar. It is somewhat sweeter than sugar, and its usefulness in the preparation of galenicals might also be looked into. Honey and manna must be mentioned. Manna is said to be especially serviceable for use with, and in the preservation of, iron preparations.

II. GLYCERIN EMERGENCY SUBSTITUTES.

The manufacture of glycerin for medicinal purposes has been discontinued in England for quite some months past, and pharmacists must be content to use whatever stocks may still be on hand. When this is used up, no further supply will be obtainable. They are looking forward to the time when they will have to do without this substance, altogether with some apprehension, for it cannot be readily replaced. They feel that the disappearance of glycerin from pharmaceutical uses would be a calamity.

In suggesting substitutes for glycerin they follow lines laid down by various investigators in Germany, where the glycerin shortage has been acute almost from the beginning of the war. Prominent among them was Dr. E. P. Unna who claims that a good glycerin substitute must have the following properties:

1—It must have fatty properties, but must not be sticky.

2—It must be hygroscopic, must not decompose at high temperature nor solidify at low temperature.

3—It must be inodorous, non-poisonous, non-irritating and have an agreeable taste.

Substitutes for glycerin are very numerous, and for simplicity's sake they may be subdivided into five classes as follows:

a—Solutions of gums, glues or other viscous substances, such as agar-agar, fish glue, Iceland moss, linseed, marshmallow root, salep, tragacanth. The principle objection to these preparations is that they require the addition of a preservative, borax, formaldehyde, etc. In this connection, I might mention that acetanilid is claimed to have been found a good preservative for mucilages. A number of preparations of such type are on the market in Germany, for example:

Lempellin, a mucilage of Irish moss preserved with borax and formaldehyde.

Algin, an infusion of laminaria stalks with sodium carbonate.

Novoglycerin, a solution of glue in water.

Glycerit, a quince seed mucilage, containing 10 percent of glycerin and a small amount of borax.

b—Solutions of sugar.—About 60 percent of sugar is required to obtain a liquid of about the same fluidity as glycerin.

c—Mixtures containing fats or oils.—Since glycerin has the advantage of freedom from greasiness, oils and fats should be present in a substitute in a diluted form, preferably emulsified. A German preparation, Proglycerin, is a diluted lanolin emulsion. Paraffin emulsions may also be used.

d—Solutions of certain salts.—These solutions are used whenever the hygroscopic property of glycerin is the one desired in the substitute. A solution of calcium chloride, 36 percent, is used for medicinal purposes. Perglycerin is a 45 percent solution of sodium lactate; Perkaglycerin a 60–80 percent solution of potassium lactate.

e—Various mixtures not classifiable under any one of the above.—A solution of magnesium chloride, 21 percent, with 60 percent glucose is claimed to be well adapted for technical purposes. A mixture of equal volumes of 2 percent gelatin solution and glycerin gave a good preparation.

We see that the range of glycerin substitutes is a very wide one indeed, but the following general considerations may help to simplify the problem before us:

1—In preparations where physiological activity depends entirely upon the presence of the glycerin, substitution should not be attempted at all. Examples of such preparations are: Glycerite of boroglycerin, glycerin suppositories, and compounds of glycerophosphates. Physicians might be requested to refrain from prescribing them.

2—In the case of preparations whose glycerin content is either small or non-essential, the glycerin might be omitted entirely or its amount might be reduced to a minimum. Examples of such preparations are: Ointment of iodine, compound tincture of gentian, mucilage of tragacanth, and others.

Glycerin is used extensively in hair tonics, face lotions and creams. To save this amount, the druggist might be advised to make a good lotion or cream of his own and to recommend it whenever glycerin is wanted for the purpose. I take the liberty of quoting you several formulae recommended by the *Chemist and Druggist.*

1—Benzoinated Lard..... 15 grains
Powdered Hard Soap..... 20 grains
Mucilage of Quince Seed... 1 1/2 ounces
Camphor Water..... 1 1/2 ounces

2—An Almond Lotion:
Almonds blanched..... 40 grains
Rose Water..... 1 1/2 ounces
Orange Flower Water..... 1 1/2 ounces
Bruise the almonds and triturate then add:
Borax..... 12 grains
Tincture of Benzoin..... 10 minims

3—Soft Soap..... 20 grains
Anhydrous Wool Fat..... 15 grains
Almond Oil..... 1/2 drachm
Water..... 2 ounces
Mucilage of Carraghean.... 1 ounce
Essence of Lily-of-the-valley 15 minims

4—A very fine cream is obtained by the following formula:
White Wax..... 1 drachm
Spermaceti..... 1 drachm
Wool Fat..... 1/2 drachm
Zinc Oxide..... 2 drachms
Spirit of Camphor..... 1/2 drachm
Radium Water..... 1/2 drachm
Cucumber Juice..... 1 ounce
Sesame Oil..... 2 1/2 ounces
Synthetic Oil of Rose..... 10 minims

I have prepared some of these creams, and have them here. They are very good indeed.

To replace glycerin in hair tonics, I find "turkey-red oil" recommended. This is sodium sulpho-ricinoleate. It is miscible with water. To replace glycerin in preparations where "body" is required, the London Pharmaceutical Committee recommends the following preparations:

Gum Tragacanth	30	grains
Chloroform	24	minims
Water, to make	10	ounces

For internal use, the following is claimed to be more suitable:

Gum Tragacanth	2	drachms
Alcohol	4	drachms
Chloroform Water	10	ounces

Another formula suggested is the following:

Picked Carragean	1	ounce
Water	25	ounces

And finally, another one:

Washed Irish Moss	1/2	ounce
Water	24	ounces

Keep boiling for fifteen minutes, strain with pressure, make up to 19 ounces with boiling water and add 1 ounce of glucose. Mix and strain.

I have prepared some of these mucilages and, they are here for your inspection. Some of those used in Germany are also included.

The subject of war emergency formulae is certainly a very important one at this time. It seems to me to be even worthy of official consideration by the American Pharmaceutical Association. War emergency formulas might be worked out by a properly constituted committee, certain definite propositions made and duly legalized. Congress would surely not stand in the way, nor would State officers refuse to coöperate. By judicious effort of this nature, the American Pharmaceutical Association would make itself of great assistance to both the government and the profession. To the government such assistance would, no doubt, be most welcome, and it would be the carrying out, in a measure, of the promise of support made to President Wilson at the outbreak of the war. To the pharmacist, advice as to what he should do and can do in this emergency would be most valuable. When common substances become scarce, the pharmacist will do the best he can (which in many instances is the worst) and, furthermore, the temptation to illegal substitution becomes great.

Let us not wait until we are asked to do it, but let us be prepared. In our national emergency don't let us be followers, let us be leaders for the country's good.

THE PREPARATION OF DICHLORAMIN T. AND CHLORINATED EUCALYPTOL 1.2.*

BY ROBERT B. KRAUSS.[1]

Para-toluol-sulphondichloramide was first prepared by Kastle, Keiser and Bradey[2] in 1896, who also prepared a number of related compounds. Since its introduction under the name of dichloramin T. by Dakin, Lee, Sweet, Hendricks and LeConte,[3] the production of this substance on a large scale in pure form, as

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EDITOR'S NOTE.—See also comment on this paper under Local Branches, this issue.

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[1] Henry Phipps Institute of the University of Pennsylvania.

[2] *American Chemical Journal*, 18, 491, 1896.

[3] *Journal American Medical Association*, 69, 27, 1917.