SUMMARY

1. A method for the determination of grain size distribution of pharmaceutical chemicals has been described.

2. The grain size distribution in two samples of Barium Sulfate have been determined.

CONCLUSIONS

It would seem that a test of this type, incorporating a limit of the per cent of large particles and a requirement for a definite per cent of small particles would be superior to the present pharmacopial test for bulkiness of powder.

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Syrup of Cranberry, A New Pharmaceutical Vehicle

*By J. A. Lubitz, C. R. Fellers and J. A. Clague**

INTRODUCTION

Any attempt to minimize a patient's discomfort and resistance to unpleasant medications is a worthy one. The increase in the number and use of efficient vehicles at the physicians service will eventually neutralize present objections to ill-tasting medicines. The trend to the use of true fruit flavors in pharmaceutical vehicles is a meritorious one. The popularity of Syrup of Cherry, N. F. VI, well illustrates this trend as does the investigation conducted by Mason (1) on grapefruit syrup and Fantus and Dyniewicz (2) on pineapple syrup.

Because of its national distribution, low cost, attractive color and pleasant flavor, the cranberry, *Vaccinium macrocarpum*, in the authors' estimation, warrants attention as the source of a potential pharmaceutical vehicle.

REVIEW OF LITERATURE

Production.—The cranberry is grown principally in Massachusetts, New Jersey, Wisconsin, Oregon and Washington. Its active marketing season extends from September to January, though cranberries are often available during winter months. The annual crop is about 50,000,000 pounds. The retail selling price is variable and depends on the total production, but is usually from $6.00 to $10.00 a barrel of 100 pounds. At retail the cost varies from 7 to 15 cents a pound.

Cranberry Syrup.—A cranberry syrup for beverage purposes was produced commercially in this country in 1895 under the name of "Ruby Phosphate." This was produced at Wareham, Massachusetts, by B. P. Waters and R. C. Randall, local pharmacists, and enjoyed a moderate sale.

Constituents.—The pure cold-pressed juice according to Rice, Fellers and Clague (3) has the following percentage composition: soluble solids 6.7, pectin (alcohol precipitate) 0.13, titrable acidity calculated as citric acid 2.60, ash 0.16 and astringency (tannin) 0.5. The p_H of this juice is 2.4, and the specific gravity is 1.058.

Isham (4) determined the nature of the acids in cranberries. The average amounts of the acids in the Early Black Variety expressed as per cent are: citric 1.1, quinic 1.0, malic 0.26 and benzoic 0.065. Nealy (5) has recently reported the presence of ursolic acid from cranberries. This substance has been used in medicine to a limited extent.

Morse (6) found the percentage composition of the ash to be: potassium oxide 0.068, sodium oxide 0.003, calcium oxide 0.018, magnesium oxide 0.009, phosphorus pentoxide 0.019, sulfur 0.005, chlorine 0.004, iron 0.00022 and manganese 0.00057. Rice, Fellers and Clague (3) found 0.00036 per cent of total iron in Early Black cranberries. The copper content varies widely, but Massachusetts cranberries contain approximately five parts per million. Isham and Fellers

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(7) found that fresh cranberries are a good source of vitamin C with 70–100 International units per ounce. The vitamin A content is from four to seven International units per ounce. Vitamins B, G and D are only in negligible amounts, if at all, in cranberries.

The anthocyan pigment responsible for the red color of cranberry juice is idæin, according to Willstatter (8), who isolated it from the German wild cranberry, *Vaccinium vitis idaea*. Tin and to a lesser extent iron containers and utensils discolor cranberry juice and darken the color first to purple and then to a brownish black. Nickel and copper also cause a slight darkening of the juice. Aluminum has no observable effect on the pigments. Long storage in flint glass bottles in the light will gradually cause the color to fade with the formation of a dark precipitate.

EXPERIMENTAL WORK

Method of Preparation.—Heat extraction of cranberry juice, though giving a higher yield, is impractical for pharmaceutical use as the pectin extracted would cause the finished syrup to jell. This could be obviated, of course, through the use of a pectin-destroying enzyme such as the commercial preparation known as Pectinol (Rohm and Haas), but the time and expense to the retail pharmacist does not warrant the use of this method. Therefore, only cold extraction methods were used in the investigation.

There were two procedures followed in compounding a cranberry syrup. In the first method 900 Gm. of cranberries were ground to a medium fineness in a food chopper, allowed to stand for one-half hour, strained through four layers of cheese cloth and filtered through coarse filter paper. The yield was 450 cc. of juice (clear and sparkling). The juice was then brought to a boil, removed from the flame and 850 Gm. of sucrose were dissolved in it. When cool the surface scum was removed, and the resulting syrup measured 950 cc.

The second method tried was similar to that given for Syrup of Cherry in the National Formulary, sixth edition. Cranberries were crushed in a food chopper, one-tenth per cent benzoic acid was added and the mixture was allowed to stand at room temperature for two days. Then the juice was expressed through four layers of cheese cloth and filtered through filter paper. The filtrate was brought to a boil, and 850 Gm. of sucrose were added to each 450 cc. of the juice. This was allowed to cool slightly, the surface scum was removed, and 20 cc. of alcohol were added to each liter of syrup.

Syrup of Cranberry prepared by the first method possessed a beautiful ruby color, the characteristic delicious cranberry flavor and a mild, pleasant aroma. This syrup when mixed with one-half its volume of alcohol showed no turbidity, indicating the absence of pectin and compatibility with alcoholic medicinal preparations. It has retained its clarity, flavor and color for over three months, the storage being in a well-lighted (sun) cabinet at room temperature.

On cooling, the cranberry syrup made by the second method, changed into a semi-solid jell. As stated previously, jelling could be avoided by removal of pectin from the juice by means of Pectinol. The first method for preparing cranberry syrup is therefore preferable and this is the syrup referred to in this paper. The jelling of syrup manufactured by the second method was thought to be due to extraction of pectin attributed to the acidity of the juice and the long maceration period.

Organoleptic Tests.—The cranberry syrup was compared with Syrup of Cherry, N. F. VI; Syrup of Raspberry, N. F. VI; Syrup of Citric Acid, U. S. P. XI; Syrup of Orange, U. S. P. XI; and Simple Syrup, U. S. P. XI.

Table I gives the results of taste tests made on the six syrups.

Table I.—Relative Palatability of Plain Flavoring Syrups—Score Sheet

Sampler	Cherry	Citric Acid	Cranberry	Simple	Raspberry	Orange
1	5	4	3	6	2	1
2	4	5	1	6	3	2
3	2	3	4	6	1	5
4	3	5	1	6	4	2
5	4	6	5	3	1	2
6	3	5	6	4	1	2
7	1	6	3	5	2	4
8	5	3	1	6	2	4
9	4	3	2	6	1	5
Score[a]	31	40	26	48	17	27

[a] Points are given to each syrup on basis of preference, *i. e.*, first choice 1 point, second choice 2 points and so on. These points are added to give a "score" so that a basis for comparison may be obtained; the lowest score being the favored syrup, the highest score being the least palatable syrup.

The palatability preference was as follows: Syrup Raspberry, first; Syrup of Cranberry, second; Syrup Orange, third; Syrup Cherry, fourth; Syrup of Citric Acid, fifth; and Simple Syrup, sixth.

Disguising Properties.—The masking properties of these syrup vehicles were tried using them as carriers for the following drugs: potassium iodide, chloral hydrate, potassium acetate, ammonium chloride and sodium citrate.

These medicinal preparations were compounded in 60 cc. amounts. The quantities of the drugs used were: potassium iodide, 5 Gm.; chloral hydrate, 5 Gm.; ammonium chloride, 5 Gm.; potassium acetate, 15 Gm.; sodium citrate, 7.5 Gm.

Potassium acetate and sodium citrate, due, no doubt, to their alkalinity, caused the red color of

cranberry syrup to change to a not unattractive light molasses color.

According to Table II, cranberry syrup ranked fifth in score as a vehicle for potassium iodide; tied in first place with Syrup of Citric Acid as a vehicle for chloral hydrate. As a masking agent for potassium acetate, cranberry again tied with Syrup of Citric Acid, this time in second place. As a vehicle for ammonium chloride it ranked in first place; and as a vehicle for sodium citrate, it ranked last.

Table II.—Relative Palatability of Drugs in Several Flavoring Syrups—Score Sheet

Drug	Sampler	Cherry	Citric Acid	Cranberry	Simple	Raspberry	Orange
Potassium iodide	1	1	6	6	2	3	6
	2	6	6	6	6	1	2
	3	2	6	5	1	3	4
	4	2	6	5	1	3	4
		11	24[b]	22[b]	10	10	16
Chloral hydrate	5	3	2	1	6	6	4
	6	2	3	4	6	5	1
	7	6	2	1	1	5	4
	8	6	2	3	3	5	4
		17	9	9	16	21	13
Potassium acetate	9	1[a]	2	6	6	6	1[a]
	10	6	2	1	4	5	3
	11	6	4	2	5	1	3
	12	4	3	2	6	4	3
		17	11	11	21	16	10
Ammonium chloride	13	2	1[a]	1[a]	6	6	2
	14	1	4	2	3	6	6
	15	5	4	3[a]	3[a]	1	2
	16	1	3	2	4	6	5
		9	12	8	16	19	15
Sodium citrate	17	3	2	5	1	6	4
	18	3	2	6	5	4	1
	19	2	5	6	3	1	4
	20	2	3	4	6	1	4
		10	12	21	15	12	13

[a] Both rated in the same place. See Table I for method of scoring.
[b] Signifies that preparation was highly objectionable and counted as 6.

SUMMARY AND CONCLUSIONS

Two methods for the preparation of cranberry syrup were tried. The method recommended for a pharmaceutical Syrup of Cranberry is one in which the juice is expressed cold, filtered, boiled and sweetened.

Potassium acetate, sodium citrate and alkalies caused a color change in this syrup.

The estimated average cost of syrup of cranberry, excluding labor, is not over 25 cents per 1000 cc.

Syrup of cranberry is an efficient vehicle for chloral hydrate, potassium acetate and ammonium chloride. It is compatible with most alcoholic preparations.

Tin, iron, nickel and copper utensils and containers cause darkening of the syrup.

Cranberry syrup is stable in color and flavor toward sunlight under ordinary storage conditions. The syrup will not spoil readily due to high sugar content, acidity and mildly bacteriostatic substances such as benzoic acid present in the cranberries.

Storage is recommended in well-filled, tightly-stoppered, amber glass containers.

It is suggested that further research on Syrup of Cranberry be carried out to ascertain its value as a carrier for other drugs.

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Ointment of Mercuric Nitrate*

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INTRODUCTION

Ointment of Mercuric Nitrate has long been in use as an antiseptic preparation and is widely employed to-day as an antiseptic application in various skin diseases such as impetigo, sycosis, ring worm and in certain forms of chronic eczema. It was originally derived from an ointment of lard and nitric acid, called Alyon's Ointment after the man who first prepared it. The Ointment of Nitric Acid of the former Edinburgh and Dublin Pharmacopœias was of this character

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