SOME NOTES ON EXTRACT OF CASCARA AND CASCARA EXTRACTION.*

BY F. W. NITARDY.

The U. S. P. IX directs extract of cascara to be made by extracting the bark with hot water, concentrating the percolate, drying the extract and finally diluting it so that one gram of extract represents three grams of the drug from which it was made.

Cascara in common with most drugs varies in the amount of extractive a perfectly dry bark will yield. According to the place in which it is stored and the prevailing weather conditions or humidity it also varies in moisture content. To adjust the extract to a definite ratio of drug, therefore, does not seem conducive to producing a preparation of uniform strength. Unfortunately, there is no practical method of determining the activity of this drug by either chemical or physiological means. However, it seems reasonable to assume that there may be a fairly definite relation between the extractive content and activity of the drug and that a more uniformly active extract would be produced if the dilution to definite drug ratio were omitted.

A questionnaire on this and other points in reference to cascara was sent to the leading pharmaceutical manufacturing houses of the country. An abstract of the questions asked and answers obtained is appended to this paper in tabulated form. It will be noted that out of five answers received to this question three state they believe the activity is proportional to extractive content. One house answers that it could establish no such relations and one believes it difficult to give an opinion because of lack of any adequate method for determining the activity of the drug or its preparations. Three other houses answering other questions made no comment on this one.

Among the diluents prescribed to be added to extract of cascara U. S. P. IX, there is a given amount of magnesium oxide. It is well known that the use of magnesium oxide as a debitterizing agent in the manufacture of aromatic fluidextract of cascara reduces the activity of this preparation to a considerable extent. The question has therefore been raised as to whether this addition of magnesium oxide to the finished powdered extract may have a detrimental effect on its efficacy as a laxative. So far as I know it is not definitely known whether the debitterizing action of magnesium oxide is due to rendering certain principles insoluble, thereby preventing their extraction, or whether they are destroyed or altered in their composition so that they lose their cathartic action and bitter taste, but are extracted along with other constituents. Further, it is not known in case they are rendered insoluble whether this affects their value therapeutically. From experience in the manufacture of the aromatic fluidextract it appears that the action of magnesium oxide is more thorough in the presence of air. That is, a better debitterizing effect is obtained if the drug is dried after mixing with water and magnesium oxide than when it is only macerated and then percolated without previous drying. This suggests that the exposure to air may facilitate whatever action or reaction takes place.

In experimental work conducted on extract of cascara it was found that this

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QUESTIONNAIRE.

Questions.	*Answers.*			
	A.	B.	C.	D.
What is the effect of MgO on cascara? Is MgO a satisfactory dilulent in extract of cascara?	Any alkali reduces activity, degree depending on strength of alkali and length of treatment.	MgO reduces activity of cascara as evidenced by debitterized preparations.	MgO lessens activity probably by combining with principles. In its addition to extract it has less chance for action. Do not use it.	MgO, CaO and other alkalis appreciably reduce activity. MgO either decomposes or renders insoluble active constituents. Do not consider its use in extract detrimental.
What is the yield of extractive—high, low and average? What is its relation to drug activity?	24–29%, average 26%. Activity of drug proportional to extractive present.	At one time judged value of bark by extractive present but abandoned this 20 yrs. ago because no relation could be established.	Average yield 25%. Hard to reach conclusion as to relation of activity to extractive content.	Well-aged dry bark yields 20–27%, average of 25% extractive.
Is there any practical method of determining activity?	No satisfactory method of determining activity except by clinical trial.	Determination of activity practically impossible except by clinical experiment.	No practical method of assay. Chemical methods not sufficiently developed; clinical tests inadequate.	Chemical method absolutely useless and unreliable. Clinical method not satisfactory. Anthraquinone derivatives no index of activity.
Is water the best menstruum? Do hydro-alcoholic menstruums give better extraction? What will such menstruum yield in extract?	Hot water best menstruum.	Water satisfactory menstruum but believe addition of 1% NH_4OH better solvent.	Water best menstruum from economic standpoint. Dil. alc. yields complete but lighter extract.	Hot water and vacuum evaporation yields active extract. Hydro-alcoholic menstruum gives more clean-cut extraction and a more fluid preparation.
	E.	F.	G.	H.
	MgO does not influence emodin content but lessens bitter principle. Doubt that it is detrimental in extract. It may combine and split up again in the body, merely a supposition.	MgO lessens activity. Its effect on extracts may be detrimental even though we have no definite evidence thereof.	MO lessens activity, not known if due to elimination of tonic effect or due to destruction of some of the active constituents. It acts on extract as shown by color change (purplish). Should not be used.	Effect of MgO on extract cannot be compared to debitterizing action in fluid-extract, as it is added to dry extract.
	Yield 25-30%. Low extractive always means low activity. Usually due to fresh bark. The latter also has tendency to gripe.	Average yield about 25%. Some yield as low as 20%, some as high as 30%. Believe activity proportional to extractive.		30–33% extractive.
		Chemical and clinical methods unsatisfactory. Clinical trial would be OK if patient could be standardized.	Clinical trial only will give index of strength.	No practical method available.
	Water is the best menstruum. 38% alcohol yields about the same amount of extractive but offers no advantage.	Hot water is a satisfactory menstruum. Alcoholic menstruums yield less extractive.	Water is the best menstruum.	Water is the best menstruum.

extract may be dried and powdered satisfactorily without the use of magnesium oxide. It is, however, somewhat difficult to accomplish this during humid weather. It was further found that if magnesium oxide is added to the soft extract previous to drying, the drying operation is accomplished very much more rapidly and easily than when the U. S. P. procedure is followed. In an effort to determine if there is any difference in therapeutic activity between extract of cascara made without the addition of magnesium oxide and that made with the addition of the amount called for by the U. S. P. both before and after drying, a given lot of cascara was extracted and the soft extract obtained divided into three portions, one portion of which was dried and brought to U. S. P. standard ratio by dilution with an inert substance. The second portion was mixed with the required amount of magnesium oxide, dried and then diluted with an inert substance to U. S. P. strength. The third portion was dried and the dried product was diluted to U. S. P. strength with magnesium oxide of the required quantity and sufficient inert material. Samples of all three were sent to our biological laboratories with the request that they be tested therapeutically by administration to animals. The report received on these tests, however, is not satisfactory or conclusive of any difference in therapeutic activity between the three products. Differences were noted but consistent results were not obtained. I tested these extracts personally but found it difficult to reach definite conclusions on their relative activity. In discussing this matter with Dr. James A. Beal at the New Orleans meeting, he kindly consented also to give these three samples of extract a personal test. I now have his report that he found all three extracts of excellent quality and, apparently, equally active.

It would probably be difficult to definitely prove that magnesium oxide is or is not detrimental to extract of cascara except by clinical tests covering thousands of cases. Should it be proved that magnesium is not in any way harmful to the product, it would certainly be desirable to add it to the moist extract before drying. In order to make sure, it may be best to omit the magnesium oxide from extract of cascara until such time as more is known on the subject, especially as its preparation without magnesium oxide offers no particular difficulty.

I have searched literature for information on the extraction of cascara but find that very little of value in connection with the manufacture of an extract or a fluidextract is available. I therefore determined to have some experiments made on the extraction of the bark for the purpose of determining what type of extractive and amount of extractive various solvents would remove from a given sample. For this purpose I selected a bag of cascara bark from stock, set half of it aside as an authentic sample, the other half I had ground and a portion of the ground drug was then extracted as follows: first, with ether, drying the marc and evaporating the ethereal percolate to a solid extract. The dried marc was then repacked and extracted with acetone. The same procedure was repeated subsequently, using alcohol, dilute alcohol and hot water as a menstruum; in each case evaporating the percolates to a dried extract and carefully drying the marc before the next extraction was attempted. On another portion of the same drug the same process was carried out in reverse order, *i. e.*, starting with hot water and ending up with ether. The results obtained from these extractions are shown on the following table, which gives the number of grams of dried extract obtained per kilo of drug used and also the percentage of the extract that was found to be water-sol-

uble. You will note that the ether extract could not be dried down to a dry solid on account of its oily nature. Further experiments along this line have been planned, but have as yet not been completed.

EXPERIMENT WITH THE EXTRACTION OF CASCARA BARK WITH A SERIES OF MENSTRUUMS.

Experiment No. 1.

Menstruum and order of extraction.	Yield of dry extract, %.	Remarks.
Ether	4.0	Bitter, tarry, insoluble in water, melts on heating.
Acetone	10.0	Bitter, 60.7% water-soluble.
Alcohol	11.0	Bitter-sweet, then acrid bitter, 82.5% water-soluble.
Dilute alcohol	9.0	Flat, faintly bitter, 83% water-soluble.
Hot water	1.7	Flat, faintly bitter, 82.2% water-soluble.
Total extractive all solvents	35.7	

Experiment No. 2.

Menstruum and order of extraction.	Yield of dry extract, %.	Remarks.
Hot water	27.0	90.8% water-soluble.
Dilute alcohol	4.5	Bitter oily taste, 63.2% water-soluble.
Alcohol	3.0	Tarry, oily taste.
Acetone	.45	Waxy, taste flat.
Ether	(.30)	Amount estimated at 0.3% extract was lost through accident in drying.
Total extractive all solvents	35.25	

One of the objects of making these experiments was to determine if some other method of removing the bitter principle from cascara would be more satisfactory than the one now employed as by the present method a large amount of the activity of the drug is lost. I have heard that one may exhaust cascara with certain organic solvents, thereby obtaining a bitter cathartic principle and rendering the bark bitterless. This bitter cathartic principle I am told is made use of under the name of Cascarin and the bitter free bark is then available for the preparation of an aromatic fluidextract. However, I have no definite information on this subject and do not know whether this practice is really followed.

Further work on this subject is under way and contemplated and I hope to make an additional report at next year's meeting.

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A COMPARISON OF CANE AND BEET SUGAR FOR PHARMACEUTICAL PURPOSES.*

BY ADRIAN THOMAS.

For a long time there has been a question, especially among manufacturers of pharmaceutical preparations, whether there is a difference between products made with a cane or beet sugar. The experiments recorded here were conducted in order to ascertain if any marked difference existed between sugars from the two sources or between solutions of them. Four samples of cane sugar and four samples of beet sugar were examined, each sample being representative of a car lot.

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