

EXPERIMENTS WITH THE PRESSURE COOKER IN DRUG EXTRACTION

By

Salvatore Joseph Greco

LIBRARY  
UNIVERSITY OF MARYLAND  
COLLEGE PARK, MD.

Thesis submitted to the Faculty of the Graduate School  
of the University of Maryland in partial  
fulfillment of the requirements for the  
degree of Doctor of Philosophy

1948

UMI Number: DP70369

All rights reserved

INFORMATION TO ALL USERS

The quality of this reproduction is dependent upon the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if material had to be removed, a note will indicate the deletion.



UMI DP70369

Published by ProQuest LLC (2015). Copyright in the Dissertation held by the Author.

Microform Edition © ProQuest LLC.

All rights reserved. This work is protected against unauthorized copying under Title 17, United States Code



ProQuest LLC.  
789 East Eisenhower Parkway  
P.O. Box 1346  
Ann Arbor, MI 48106 - 1346

#### ACKNOWLEDGEMENTS

The author wishes to express his sincere appreciation and gratitude to the following for their aid in this work:

To Dean Andrew G. Dulles, under whose guidance the investigation was carried out.

To Dr. Clifford W. Chapman, for his advice concerning the assay of Digitalis Tincture.

To Mr. Paul R. Young, for his immeasurable aid in the laboratory work on the assay of Digitalis Tincture.

## CONTENTS

	Page
INTRODUCTION	1
EXPERIMENTAL	4
Description of Apparatus	4
Method of Operation of Cooker	5
Official Extraction Methods Used	6
Physical Constants and Properties of the Preparations	9
Determination of Total Extractive	10
Assays	10
Extraction of Specific Drugs	
1. Nux Vomica	11
2. Belladonna Leaf	20
3. Hyoscyamus	23
4. Stramonium	25
5. Ginger	27
6. Ipecac	30
7. Cascara Sagrada	33
8. Wild Cherry	35
9. Digitalis	38
DISCUSSION	46
CONCLUSIONS	49
REFERENCES	51

## TABLES

Table No.	Page
I.- The Relationship between Percentage Mortality and the Curve Number for Digitalis Tincture	40
II.- Physical Properties - Color, Odor, Taste and Changes on Storage of the Preparations Made	43
III.- Specific Gravities of the Preparations Made	44
IV.- pH Values of the Preparations Made	44
V.- Total Extractive and Alkaloidal Content of the Preparations	45

## INTRODUCTION

Few, if any, ideas pertaining to new methods of extraction of vegetable drugs have been advanced in recent years. A survey of the available literature failed to reveal any attempt to develop new methods of extraction, but showed on the contrary that the work which was done in this field, had as its objective the improvement of the percolation methods which have been used for many years.

Shortly before the beginning of World War II, there appeared on the market in this country a household pressure cooker, by the use of which, foods could be cooked in approximately one-third of the usual time.

In 1843 Isaac Winslow (1), a canner from Maine, in trying to improve upon food processing methods in use at that time, experimented with a small copper boiler which forced steam at 12 pounds per square inch into a steam tight tank lined with zinc. The results obtained were not encouraging and the experiments were discontinued. In 1846 (1), M. Raymond Chevallier-Appert of France devised an autoclave, or steam chamber, for processing canned foods. A manometer was attached to it to record variations of pressure. The first pressure cooker for processing foods on a commercial scale made in America was devised by Andrew K. Shriver (2) of Baltimore in 1874. Actually Mark O. Shriver, a partner in, and cannery operator for T. J. Ayer and Company, originated it, but his senior partner, A. K. Shriver, was granted the patent on it. This new invention was called and is still called a "Shriver Kettle". It is said that this kettle revolutionized the canning industry.

The first pressure cooker intended for household use made its appearance as early as 1938, but the general public was skeptical, and it was some time before its usefulness in the home was established. World War II brought about a tremendous increase in the spread of its use. The Government was urging the people to aid the war effort by canning their own foods, thus enabling the industrial canners to divert more of their goods to the Armed Forces. By the use of the pressure cooker, home-canning could be accomplished in less time and with greater convenience than by the methods ordinarily used. However, the production of the cookers during the war was limited because of the war-time restrictions on the use of metals necessary for their manufacture. After the cessation of hostilities, the restrictions on the use of metals in the industries were removed, and these cookers began to be manufactured on a large scale. Today, there are several types available, and their use has spread to all sections of the country. They are comparatively inexpensive. A satisfactory cooker for use in the home can be purchased for \$8.95 to \$19.95, depending upon its capacity.

If time could be saved in the cooking of fresh vegetable matter by this method, it seemed to be logical to assume that if the tissues of a dried drug were moistened beforehand and the drug then cooked in a pressure cooker with the proper menstruum, the active principles would be extracted in a shorter period of time than by the methods now in general use. However, there was some doubt as to the feasibility of the method, because many of the active principles of drugs are heat labile and might undergo change or decomposition in the process of cooking. Nevertheless, it was believed to be worth the effort to determine if extraction by this method would be practicable. Therefore, the experiments described herein were undertaken.

These experiments were limited to the preparation of some of the more important types of tinctures and fluidextracts official in the Pharmacopoeia of the United States, XIII, and the National Formulary, VIII. The official preparations and those made by the pressure cooker method were compared with respect to specific gravity, pH value, color of the freshly prepared product, appearance of the preparation after storage for 6 months, odor, taste, total extractive and alkaloidal content. With the exception of the alkaloidal content, all of these comparisons were made after final adjustment of the preparation to official standards.



## EXPERIMENTAL

## Description of Apparatus

The pressure cookers intended for household use on the market today are constructed principally of metal, usually aluminum or stainless steel. Their capacities range from 1 1/2 to 6 quarts. The handles may be composed of plastic or bakelite. The gasket are made of synthetic composition or neoprene rubber. Some types of cookers have outside closures; others have inside closures.

Safety devices are an important feature of the pressure cooker. In most cases the safety plug is located in the cover of the cooker and will release, if the steam vent becomes clogged.

Some manufacturers provide for a range of 5, 10, and 15 pounds of pressure per square inch in their cookers, but many types are designed to maintain a constant pressure of 15 pounds, because it has been found that this pressure is the most satisfactory for all purposes. Various types of pressure controls are used. Some cookers are equipped with tension springs, which are set to release vapor at the desired pressure. Others are equipped with a calibrated weight, which permits just sufficient vapor to escape in order to maintain the pressure at a constant level.

The body of the pressure cooker used in these experiments is made of stamped aluminum and has a capacity of 4 quarts. The handles are composed of heat-proof plastic. The gasket is constructed of neoprene rubber. It has an outside closure; the cover locks onto the body by notching lips. The cooker is locked by handle action with the gasket completing the seal. Its pressure range is 5, 10, 15 pounds, controlled by the position of the

calibrated weight over the steam vent. The jiggling of the weight shows that the desired pressure has been reached. This type of cooker is provided with a number of safety devices, viz.: the safety plug in the cover melts with excessive heat or releases with excessive pressure, if the pan cooks dry or the vent clogs. The gasket is built to release excessive pressure downward in the event that the safety plug should fail. The weight of the metal can withstand more than seven times the recommended cooking pressure.

#### Method of Operation of Cooker

The drug is weighed, placed in the pressure cooker, and after the addition of a calculated amount of menstruum, macerated for 15 minutes. The cooker is then closed, and the pressure control placed over the vent tube at the number 15 hole, indicating that 15 is the number of pounds of pressure desired. The cooker is then placed on a tripod over a Bunsen burner with a high flame. When the desired pressure is reached, the pressure control will jiggle and sputter constantly. The cooking time is counted from this moment, the time in most of these experiments being 10 minutes. The flame is reduced so that the control jiggles only about three times per minute. It should not jiggle more frequently than this if the loss of an excessive amount of menstruum, causing the drug to cook dry or even burn, is to be avoided. After the desired pressure had been maintained for 10 minutes, the cooker is removed from the tripod and placed under a stream of cold water to reduce the pressure. After the pressure registers zero, the pan is opened and its contents filtered through cotton in an ordinary glass funnel. When the filtrate begins to come through clear, return the filtrate to the funnel and continue the filtration until an amount equal to that specified in the Pharmacopoeia of the United States, XIII, or

National Formulary, VIII, for assayed tinctures or fluidextracts, has been collected. If necessary, a sufficient quantity of menstruum is added through the filter to produce the desired amount of filtrate. The product is then assayed. Upon different occasions modifications of the above procedure were performed. They will be noted throughout the discussion.

Hereafter, the abbreviation, U.S.P., XIII, will be used to designate the Pharmacopoeia of the United States, XIII, and N.F., VIII, will be used to designate the National Formulary, VIII.

#### Official Extraction Methods Used

The official tinctures and fluidextracts used in these experiments for comparison with those made by the cooker method were prepared in accordance with the official methods described in the following paragraphs.

U.S.P., XIII, and N.F., VIII, Process P. All the tinctures prepared for use in these experiments were made by Process P of the U.S.P., XIII, and the N.F., VIII (h). This process is as follows:

"Carefully mix the ground drug or mixture of drugs with a sufficient quantity of the prescribed menstruum to render it evenly and distinctly damp, allow it to stand for 15 minutes, transfer it to a suitable percolator, and pack the drug firmly. Pour on enough of the prescribed menstruum to saturate the drug, cover the top of the percolator, close the lower orifice, and allow the drug to macerate for 24 hours or for the time specified in the monograph. If no assay is directed, allow the percolation to proceed slowly, or at the specified rate, gradually adding sufficient menstruum to produce 1000 cc. of tincture, and mix thoroughly. If an assay is directed, collect only 950 cc. of percolate, mix this thoroughly, and assay a portion of it as

directed. Dilute the remainder with such a quantity of the prescribed menstruum as calculation from the assay indicates is necessary to produce a tincture that conforms to the prescribed standard. Mix well."

U.S.P., XIII, and N.F., VIII, Process A. Ginger Fluidextract was prepared by Process A of the U.S.P., XIII, and the N.F., VIII (5). "This process is used for preparing fluidextracts which are made with menstrua of alcohol or with mixtures of alcohol and water, by ordinary percolation." Process A is as follows:

"Carefully mix 1000 Gm. of the ground drug with a sufficient quantity of the prescribed to render it evenly and distinctly damp. This usually requires from 600 cc. to 800 cc. of menstruum. Allow the dampened drug to stand for about 15 minutes, then pack it firmly in a suitable percolator, and pour on sufficient menstruum to saturate the drug and leave a stratum above. When the liquid is about to drop from the percolator, close the lower orifice, cover the percolator, and allow the drug to macerate for about the prescribed period of time. Then proceed with the percolation at the specified rate, adding fresh menstruum as needed until the drug is exhausted of its active principles. Reserve the first 850 cc. of the percolate (unless otherwise directed in the formula), recover the alcohol from the percolate subsequently collected, and concentrate the residue to a soft extract at a temperature not exceeding 60°C. Dissolve this extract in the reserved percolate, and, if no assay is directed, add enough of a mixture of alcohol and water to make the fluidextract measure 1000 cc. and contain the required proportion of alcohol. Mix thoroughly. If the fluidextract being prepared is to be adjusted to a standard, assay a portion of the reserved percolate in which the soft extract has been dissolved, and dilute the remainder to the volume determined as necessary by calculation

from the assay, using a sufficient quantity of an alcohol and water mixture to provide the required proportion of alcohol. Mix thoroughly."

U.S.P., XIII, and N.F., VIII, Process B. Nux Vomica Fluidextract was prepared by Process B of the U.S.P., XIII, and the N.F., VIII (6). "This process is used in preparing fluidextracts, portions of the menstrua for which contain, in addition to alcohol, or a mixture of alcohol and water, definite quantities of other components such as an acid or glycerin, the two menstrua being successively employed." Process B is as follows:

"Carefully mix 1000 Gm. of the ground drug with a special quantity of Menstruum I (containing the special ingredient) to render it evenly and distinctly damp. From 600 cc. to 800 cc. of menstruum is usually required. Allow the dampened drug to stand for about 15 minutes, then pack it firmly in a suitable percolator and pour on the remainder of Menstruum I. When the liquid is about to drop from the percolator, close the lower orifice, cover the percolator, and allow the drug to macerate for about the prescribed period of time. Then proceed with the percolation at the specified rate, and when the first menstruum has disappeared from the surface of the drug, use Menstruum II as needed until the drug is exhausted of its active principles. Reserve the first 850 cc. of percolate, recover the alcohol from the percolate subsequently collected, and evaporate the residue to a soft extract at a temperature not exceeding 60° C. Dissolve this extract in the reserved percolate, and if no assay is directed, add enough of a mixture of alcohol and water to make the fluidextract measure 1000 cc. and contain the required proportion of alcohol. Mix thoroughly. If the fluidextract being prepared is to be adjusted to a standard, assay a portion of the reserved percolate in which the soft extract has been dissolved, and dilute the remainder to a volume determined as necessary by the calculation from the

assay, using a sufficient quantity of an alcohol and water mixture to provide the required proportion of alcohol. Mix thoroughly."

U.S.P., XIII, and N.F., VIII, Process D. Cascara Sagrada Fluidextract was prepared by Process D of the U.S.P., and the N.F., VIII (7). "This process is used for preparing fluidextracts with boiling water as the menstruum, alcohol being added as a preservative to the concentrated percolate." Process D is as follows:

"To 1000 Gm. of the coarsely ground drug add about 3000 cc. of boiling water, mix well, and allow it to macerate in a suitable, covered metallic percolator for 2 hours. Then allow the percolation to proceed at the specified rate, gradually adding boiling water until the drug is exhausted. Evaporate the percolate on a water bath, or in a vacuum still, to the volume specified, cool, add the alcohol, and allow the mixture to stand in a stoppered container for several days. Then decant the clear liquid, filter the remainder into the decanted liquid, and wash the residue on the filter with a sufficient quantity of a mixture of alcohol and water to make the fluidextract measure 1000 cc. and contain the required proportion of alcohol. Mix thoroughly."

#### Physical Constants and Properties of the Preparations

Physical Properties. The physical properties studied included odor, taste, color of the freshly prepared product, and appearance after storage for six months. These values appear in Table No. II.

Specific Gravity. This constant was determined with a Mohr-Westphal balance at 25° C., and the values are reported in Table No. III.

pH Values. These were determined with a Beckman pH Meter and are reported in Table No. IV.

### Determination of Total Extractive

The U.S.P., XIII, method for determining the diluted alcohol-soluble extractive (8) was used for the determination of total extractive. The method used is as follows:

Measure accurately 50 cc. of the preparation into a tared beaker by means of a pipette. The beaker had been previously heated to constant weight in an oven at 110° C. Evaporate the sample to dryness over a water bath and dry to constant weight at 110° C. These values are shown in Table No. V.

### Assays

All of the preparations were assayed by the official methods directed for the drugs used. These values appear in Table No. V.

## Extraction of Specific Drugs

## 1. Nux Vomica

Preparation of Nux Vomica Tincture No. 1, N.F., VIII (9), by Process P.

The formula for preparing this tincture is as follows:

Nux Vomica, in moderately coarse powder . . . . .	100 Gm.
Alcohol,	
Hydrochloric Acid,	
Water, each, a sufficient quantity,	
To make about . . . . .	1000 cc.

The Tincture was prepared by Process P (4), as modified for assayed tinctures. Macerate the drug during 24 hours in a mixture of 7.5 cc. of hydrochloric acid, 150 cc. of alcohol, and 42.5 cc. of water, then percolate slowly, using a mixture of 3 volumes of alcohol and 1 volume of distilled water as the menstruum. Keep the Tincture at a temperature of 5° C. for 30 minutes, and filter."

The Tincture was assayed by the official method (9). "Measure accurately 100 cc. of Nux Vomica Tincture and evaporate it at a temperature not exceeding 100° C. to a volume of about 20 cc. Transfer the concentrated liquid to a separator containing about 30 cc. of chloroform, rinse the container with about 20 cc. of diluted alcohol, and add the rinsings to the separator. Then add 20 cc. of distilled water and 5 cc. of ammonia T. S., and shake the mixture thoroughly for 1 minute. Draw off the separated chloroform solution, and completely extract the alkaloids from the alkaline liquid by shaking it with successive portions of chloroform. Combine the chloroform solutions and add about 40 cc. of approximately 1 N. sulfuric acid to the separator, and shake the mixture gently for 5 minutes, then allow the liquids to separate, and draw off the acid into another separator. Repeat the



extraction with successive portions of the acid, until the chloroform solution is completely extracted.

To the combined acid solutions in the separator add a small piece of red litmus paper and 50 cc. of chloroform, and follow with sufficient ammonia T.S. to render the aqueous layer alkaline, and after gently shaking, add 2 or 3 cc. more of the ammonia T.S. Now shake the mixture thoroughly, but gently, for about 10 minutes, and allow the liquids to separate. Draw off the chloroform into a container, and repeat the extraction with additional portions of chloroform until all of the alkaloid is extracted. Extract the combined chloroform solutions with successive portions of approximately 1 N sulfuric acid until completely extracted. Then render the combined acid solutions alkaline with ammonia T.S., add 2 or 3 cc. more of the ammonia T.S., and completely extract the alkaloids with successive portions of chloroform.

Completely evaporate the combined chloroform extracts to dryness on a water bath, dissolve the residue by warming with 15 cc. of approximately 3 % sulfuric acid, cool to 25° C., and add 3 cc. of a mixture of equal parts of nitric acid and a 5 % solution of sodium nitrite in distilled water. Thoroughly stir this mixture, and allow it to stand for exactly 10 minutes at room temperature. At the expiration of this period, pour the red solution at once into a separator containing 50 cc. of chloroform and 15 cc. of sodium hydroxide solution (1 in 10), and rinse the flask with distilled water, adding the rinsings to the separator. Add sufficient sodium hydroxide solution (1 in 10), to the contents of the separator to render it distinctly alkaline to litmus paper, and then add a few cc. more of the sodium hydroxide solution. Shake the mixture gently for 10 minutes and allow the liquids to separate. Draw off the chloroform layer into another separator and repeat the extraction with additional portions of chloroform until the alkaloid is completely removed.

Add 10 cc. of distilled water to the combined chloroform extract, shake the mixture gently, and add a small piece of red litmus paper. The litmus paper should indicate not more than a slight alkalinity. If the water, after shaking with the chloroform, is strongly alkaline, draw off the chloroform, and shake it with another 10 cc. of distilled water. Draw off the chloroform, passing it through a filter paper moistened with chloroform, into a container. Wash the filter paper with warm chloroform, and add these rinsings to the container. Now shake the combined aqueous extract with 5 cc. of chloroform and draw off this chloroform, passing it through the chloroform-moistened filter paper into the main chloroform solution.

Evaporate the combined chloroform extracts very carefully on a water bath nearly, but not quite, to dryness. Add to the moist residue 7 cc. of 0.1 N sulfuric acid accurately measured, followed with 30 cc. of distilled water, and heat the mixture on a water bath until the alkaloid is dissolved and the odor of chloroform is dissipated. Cool to room temperature, and titrate the excess acid with 0.02 N sodium hydroxide, using 1 drop of methyl red T.S. as the indicator. Each cc. of 0.1 N sulfuric acid is equivalent to 0.0334 Gm. of strychnine."

The results of the assay gave 0.1252 Gm. of strychnine in 100 cc. of the Tincture. The Tincture was then adjusted by the addition of sufficient of a mixture of 0.8 cc. of hydrochloric acid, 75 cc. of alcohol, and 24.2 cc. of water to make each 100 cc. contain 0.111 Gm. of strychnine. After adjustment the physical properties were determined with the following results:

Specific gravity .... 0.8872  
 pH value ..... 1.70  
 Color of the fresh preparation .. Orange  
 Odor .... Wine-like  
 Taste ... Very bitter  
 Total extractive .... 1.3776 Gm. per 100cc.

Nux Vomica Tincture No. 2, Prepared by the Pressure Cooker Method

(Maceration Procedure). The following formula was used:

Nux Vomica, in moderately coarse powder.....	40 Gm.
Hydrochloric Acid.....	3 cc.
Alcohol.....	285 cc.
Water.....	92 cc.

The nux vomica was weighed and placed in the pressure cooker. The hydrochloric acid, alcohol, and water were mixed and poured over the drug, and it was allowed to macerate for 24 hours in the closed cooker. The mixture was then cooked for 5 minutes at 15 pounds pressure. It was cooled and filtered through cotton. Enough of a mixture of 3 volumes of alcohol and 1 volume of water was passed through the filter to make the final product measure 380 cc. The Tincture was cooled at 5° C. for 30 minutes and filtered. The Tincture thus prepared could not be clarified either before or after defatting.

Even though the Tincture could not be clarified, it was assayed according to the official N.F., VIII, method (9), and gave 0.1133 Gm. of strychnine per 100 cc. of Tincture.

Nux Vomica Tincture No. 3, Prepared by the Pressure Cooker Method (Non-

Maceration Procedure). The following formula was used:

Nux Vomica, in moderately coarse powder.....	40 Gm.
Hydrochloric Acid.....	3 cc.
Alcohol.....	285 cc.
Water.....	92 cc.

The nux vomica was weighed and placed in the pressure cooker. The hydrochloric acid, alcohol, and the water were mixed and poured over the drug, and it was allowed to macerate for 15 minutes. The mixture was then cooked for 10 minutes at 15 pounds pressure. It was cooled and filtered through cotton. Enough of a mixture of 3 volumes of alcohol and 1 volume of water was passed through the filter to make the final product measure

380 cc. The Tincture was kept at a temperature of 5° C. for 30 minutes and filtered. This tincture also could not be clarified.

The Tincture, when assayed by the official method (9), gave 0.1167 Gm. of strychnine per 100 cc. of Tincture.

Based on the results obtained in the assays of the two tinctures, the maceration procedure showed no advantage over the non-maceration procedure. Consequently, the non-maceration procedure was used sparingly throughout the remainder of all of the extraction experiments.

Nux Vomica Tincture No. 4, Prepared by the Pressure Cooker Method (Acetic Acid Menstruum - 15 Pounds for 5 Minutes). Since the tinctures obtained by the use of hydrochloric acid in the menstruum could not be clarified, various modifications of this method were tested. The U.S.P., X (10), directed the use of acetic acid instead of hydrochloric acid as part of the menstruum for making the Tincture; therefore, the following modification was tried:

Nux Vomica, in moderately coarse powder.....	40 Gm.
Acetic Acid.....	5 cc.
Alcohol.....	325 cc.
Water.....	105 cc.

The nux vomica was weighed and placed in the pressure cooker. The acetic acid, alcohol, and water were mixed and poured over the drug. This mixture was allowed to macerate for 15 minutes, after which it was cooked for 5 minutes at 15 pounds pressure. The contents of the cooker was filtered through cotton. Enough of a mixture of 3 volumes of alcohol and 1 volume of water was passed through the filter to measure 380 cc. The Tincture was kept at a temperature of 5° C. for 30 minutes and filtered. The Tincture thus obtained was a perfectly clear, light yellow liquid with a wine-like odor and a very bitter taste. It was assayed according to the official method (9).

However, it gave only 0.0855 Gm. of strychnine per 100 cc. of Tincture.

Nux Vomica Tincture No. 5, Prepared by the Pressure Cooker Method (Acetic Acid Menstruum - 15 Pounds for 10 Minutes). Since, in the foregoing

experiment, a low yield of strychnine was obtained, another experiment was run to determine if an increase in the length of the cooking period would yield a greater amount of strychnine. The formula used is identical with that used in the foregoing experiment, the only difference being that the cooking time has been increased from 5 minutes to 10 minutes in this experiment.

The Tincture when assayed gave 0.111 Gm. of strychnine per 100 cc. of Tincture. Its physical properties were found to be as follows:

Specific gravity.....	0.8999
pH value.....	5.15
Color of the fresh preparation.....	Clear yellow
Odor.....	wine-like
Taste.....	Very bitter
Total extractive.....	1.3050 Gm. per 100 cc.

At this point a comparison was made between the last tincture prepared by the cooker process and that made by the official method. Both tinctures conformed to the official standards with respect to alkaloidal content. The N.F., VIII (9), states that the Tincture should be adjusted so that each 100 cc. of the Tincture contains 0.115 Gm. of strychnine. However, the Tincture made by the pressure cooker method contained only 0.111 Gm. of strychnine. Therefore, for the sake of comparison of the total extractive, pH value, and specific gravity, the products were adjusted so that each tincture contained 0.111 Gm. of strychnine per 100 cc., this strength still conforming to the N.F., VIII, standards. Their specific gravities were within a comparatively close range of each other. Their pH values demonstrated considerable difference. This was no doubt due to the fact that hydrochloric acid was used in the official Tincture, whereas acetic acid was used

in the Tincture made by the pressure cooker method. A particularly good feature of the Tincture made by the cooker method was the fact that it contained less total extractive than the official Tincture. This is highly desirable, because most of the total extractive is composed of inert material. A great variation in color was noticed between the two tinctures, the official one having an orange color, whereas the Tincture prepared by the cooker process possessed a light yellow color. Probably the greatest advantage possessed by the cooker method is the fact that it is a great time-saver. Only 2 hours were required for the preparation of the Tincture by the cooker method, whereas 30 hours were required to make the Tincture by the official method.

In view of these results, it was concluded that the pressure cooker method was satisfactory for the manufacture of Nux Vomica Tincture and has a distinct advantage over the official method in the saving of time.

Preparation of Nux Vomica Fluidextract, N.F., VIII (11). Nux Vomica Fluidextract was prepared by Process B (6), as modified for assayed fluid-extracts. "Use a mixture of 2 volumes of acetic acid, 3 volumes of water, and 15 volumes of alcohol as Menstruum I, and a mixture of 3 volumes of alcohol and 1 volume of water as Menstruum II; macerate the drug during 48 hours, and percolate at a moderate rate. Chill the percolate until the fat is separated, and filter while cold."

The product obtained was dark reddish-brown in color, and it had a wine-like odor and a very bitter taste.

The Fluidextract was assayed according to the official method (11), which is as follows:

"Transfer 10 cc. of Nux Vomica Fluidextract, accurately measured, to a separator containing about 30 cc. of chloroform, add 5 cc. of water and

5 cc. of ammonia T.S.; and shake well for 1 minute. Draw off the separated chloroform solution, and complete the extraction of the alkaloids from the alkaline liquid by shaking with successive portions of chloroform. Combine the chloroform solutions and complete the assay as directed under Nux Vomica (12), beginning with 'Add about 40 cc. of approximately 1 N sulfuric acid....' Each cc. of 0.1 N sulfuric acid is equivalent to 0.03344 Gm. of strychnine."

The assay gave 1.264 Gm. of strychnine per 100 cc. of Fluidextract.

#### Preparation of Nux Vomica Fluidextract by the Pressure Cooker Method.

The following formula was used for the preparation of Nux Vomica Fluidextract:

Nux Vomica, in moderately coarse powder.....	400 Gm.
Acetic Acid.....	40 cc.
Water.....	185 cc.
Alcohol.....	675 cc.

The nux vomica was weighed and placed in the pressure cooker. The acetic acid, water, and alcohol were mixed and poured over the drug. The mixture was allowed to macerate for 24 hours in the closed cooker. The mixture was then cooked for 5 minutes at 15 pounds pressure. The contents of the cooker was cooled and filtered through cotton. Enough of a mixture of 3 volumes of alcohol and 1 volume of water was passed through the filter to measure 340 cc. The percolate was chilled until the fat was separated and filtered while cold.

The product obtained was light reddish-brown in color, and it had a wine-like odor and a very bitter taste. The Fluidextract was assayed according to the official method (11) and (12). Only 0.3912 Gm. of strychnine was found per 100 cc. of Fluidextract.

In the case of the pressure cooker method, the nux vomica was not exhausted, as was the case in the official method. Only 340 cc. of the

filtrate was collected by the pressure cooker method. This was done in order to determine the amount of strychnine which could be extracted from the nux vomica by the cooker method without exhausting the drug. Consequently, in order to make such a comparison, the final volumes would necessarily have to be identical.

In view of the low alkaloidal content of the Fluidextract just prepared, it was evident that the total strychnine could not be extracted from the drug in one operation; therefore, no further experiments were conducted along this line.



## 2. Belladonna Leaf

Preparation of Belladonna Tincture, U.S.P., XIII (13), by Process P. The formula used in making this official tincture is as follows:

Belladonna Leaf, in fine powder.....	40 Gm.
To make about.....	400 cc.

This tincture was prepared by Process P (4), using a mixture of 3 volumes of alcohol and 1 volume of water as the menstruum.

The Tincture was assayed by the official method (14). "Measure accurately 100 cc. of Belladonna Tincture, and evaporate it on a water bath to a volume of about 10 cc. Transfer the concentrated liquid to a separator containing 25 cc. of chloroform, rinse the container with small portions of diluted alcohol, and add the rinsings to the separator. Add 25 cc. of water, and render the mixture alkaline by the addition of ammonia T.S.; then completely extract the alkaloids with successive portions of chloroform. Completely remove the alkaloids from the immiscible solvent by extracting with successive portions of approximately half-normal sulfuric acid, filtering each portion drawn off. Render the combined acid solutions distinctly alkaline with ammonia T.S., and completely remove the alkaloids at once by extracting with successive portions of chloroform. Evaporate the combined chloroform extracts to dryness on a water bath and then heat in a bath of boiling water for 15 minutes. Dissolve the residue in a small volume of chloroform, evaporate to dryness on a water bath, and heat in a bath of boiling water for 15 minutes. Dissolve the resulting residue in a few cc. of chloroform, add 15 cc. of fiftieth-normal sulfuric acid, remove the chloroform by evaporation, cool and titrate the excess acid with fiftieth-normal sodium hydroxide, using methyl red T.S. as the indicator. Each cc. of fiftieth-normal

acid is equivalent to 5.787 mg. of the alkaloids of Belladonna Leaf."

The results of the assay showed 50.36 mg. of the alkaloids of belladonna leaf in 100 cc. of the Belladonna Tincture. The Tincture was then adjusted so that 100 cc. of it would contain 30 mg. of the alkaloids of belladonna leaf. After adjustment the physical properties were determined with the following results:

Specific gravity.....	0.8840
pH value.....	6.27
Color of fresh preparation.....	Dark greenish brown
Odor.....	Tobacco-like
Taste.....	Alcoholic
Total extractive.....	1.1394 Gm. per 100 cc.

Belladonna Tincture Prepared by the Pressure Cooker Method. The formula

used in making this tincture is as follows:

Belladonna Leaf, in fine powder.....	40 Gm.
Alcohol.....	325 cc.
Water.....	110 cc.

The belladonna leaf was weighed and placed in the pressure cooker. The alcohol and water were mixed and poured over the drug. The mixture was allowed to macerate for 15 minutes and was then cooked for 10 minutes at 15 pounds pressure. The contents of the cooker was filtered through cotton. Enough of a mixture of 3 volumes of alcohol and 1 volume of water was passed through the filter to measure 380 cc.

The Tincture was assayed according to the official method (14). The assay gave 50.36 mg. of the alkaloids of belladonna leaf in 100 cc. of the Tincture. Thus, the two tinctures made by the two different processes were identical in alkaloidal content.

The Tincture was then adjusted so that 100 cc. of it would contain 30 mg. of the alkaloids of belladonna leaf. After adjustment, the physical properties were determined with the following results:

Specific gravity.....	0.8950
pH value.....	6.32
Color of fresh preparation.....	Dark greenish brown
Odor.....	Tobacco-like
Taste.....	Alcoholic
Total extractive.....	0.9992 Gm. per 100 cc.

A comparison of the two tinctures is now possible. The alkaloidal strengths are identical. The specific gravities and pH values are within a comparatively close range of each other. The total extractive is less in the Tincture made by the cooker method. The time required to make the Tincture by the cooker method was 3 hours, whereas 30 hours were required to make the Tincture by the official process.

In view of this comparison it can readily be seen that the two tinctures are similar in almost every respect. However, the Tincture made by the cooker method must be considered superior, because it contains less total extractive than the official Tincture, indicating greater stability or keeping qualities. Therefore, it was concluded that the pressure cooker method is superior to the official method for the manufacture of Belladonna Tincture.

## 3. Hyoscyamus

Preparation of Hyoscyamus Tincture, U.S.P., XIII (15), by Process P. The formula used in making this official tincture is as follows:

Hyoscyamus, in fine powder.....	40 Gm.
To make about.....	100 cc.

This tincture was prepared by Process P (4), using a mixture of 3 volumes of alcohol and 1 volume of water as the menstruum.

The Tincture was assayed by the official method (16). "Measure accurately 250 cc. of the Tincture, and evaporate it at a temperature not exceeding 100° C., to a volume of about 25 cc. Complete the assay as directed under Belladonna Tincture (13), beginning with the words 'Transfer the concentrated liquid.' Each cc. of fiftieth-normal acid is the equivalent of 5.787 mg. of the alkaloids of hyoscyamus.

The results of the assay showed 4.95 mg. of the alkaloids of hyoscyamus in 100 cc. of the Hyoscyamus Tincture. The Tincture was then adjusted so that 100 cc. of it would contain 4 mg. of the alkaloids of hyoscyamus. After adjustment the physical properties were determined with the following results:

Specific gravity.....	0.8880
pH value.....	6.05
Color of fresh preparation.....	Dark greenish brown
Odor.....	Tobacco-like
Taste.....	Slightly pungent
Total extractive.....	1.7896 Gm. per 100 cc.

Hyoscyamus Tincture Prepared by the Pressure Cooker Method. The formula used in making this tincture is as follows:

Hyoscyamus, in fine powder.....	40 Gm.
Alcohol.....	375 cc.
Water.....	125 cc.

The hyoscyamus was weighed and placed in the pressure cooker. The alcohol and water were mixed and poured over the drug. The mixture was allowed to macerate for 15 minutes and was then cooked for 10 minutes at 15 pounds pressure. The contents of the cooker was filtered through cotton. Enough of a mixture of 3 volumes of alcohol and 1 volume of water was passed through the filter to measure 380 cc.

The Tincture was assayed according to the official method (16). The results of the assay showed 5.19 mg. of the alkaloids of hyoscyamus in 100 cc. of the Tincture. The Tincture was then adjusted so that 100 cc. of it would contain 4 mg. of the alkaloids of hyoscyamus. After adjustment the physical properties were determined with the following results:

Specific gravity.....	0.8992
pH value.....	6.12
Color of fresh preparation.....	Darker greenish brown than the official Tincture.
Odor.....	Tobacco-like
Taste.....	Slightly pungent
Total extractive.....	1.485 Gm. per 100 cc.

A comparison of the two tinctures was made. The alkaloidal strength of the Tincture made by the cooker method is slightly higher than that made by the official method. The specific gravities and pH values are within a comparatively close range of each other. The total extractive of the pressure cooker Tincture is less than that made by the official method. The time required to make the Tincture by the pressure cooker method was 3 hours, whereas 30 hours were required to make the Tincture by the official method.

From this comparison it can be seen that the Tincture made by the pressure cooker method is superior in all respects to that made by the official process.

## 4. Stramonium

Preparation of Stramonium Tincture, U.S.P., XIII (17), by Process P. The formula used in making this official tincture is as follows:

Stramonium, in fine powder.....	40 Gm.
To make about.....	400 cc.

This tincture was prepared by Process P (4), as modified for assayed tinctures, using a mixture of 3 volumes of alcohol and 1 volume of water as the menstruum. Percolate the drug at a moderate rate.

The Tincture was assayed by the official method (18). Measure accurately 100 cc. of Stramonium Tincture and evaporate it, at a temperature not exceeding 100° C., to a volume of about 10 cc. Complete the assay as directed under Belladonna Tincture (13), beginning with the words 'Transfer the concentrated liquid to a separator.' Each cc. of fiftieth-normal is equivalent to 5.787 mg. of the alkaloids of stramonium.

The results of the assay showed 42.7 mg. of the alkaloids of stramonium in 100 cc. of the Stramonium Tincture. The Tincture was then adjusted so that 100 cc. of it would contain 25 mg. of the alkaloids of stramonium. After adjustment the physical properties were determined with the following results:

Specific gravity.....	0.8853
pH value.....	6.17
Color of fresh preparation.....	Dark greenish brown
Odor.....	Slightly tobacco-like
Taste.....	Pungent
Total extractive.....	1.5686 Gm. per 100 cc.

Stramonium Tincture Prepared by the Pressure Cooker Method. The formula used in making this tincture is as follows:

Stramonium, in fine powder.....	40 Gm.
Alcohol.....	325 cc.
Water.....	110 cc.

The stramonium was weighed and placed in the pressure cooker. The alcohol and water were mixed and poured over the drug. The mixture was allowed to macerate for 15 minutes and was then cooked for 10 minutes at 15 pounds pressure. The contents of the cooker was filtered through cotton. Enough of a mixture of 3 volumes of alcohol and 1 volume of water was passed through the filter to measure 380 cc.

The Tincture was assayed according to the official method (18). The results showed 36.1 mg. of the alkaloids of stramonium in 100 cc. of the Tincture. The Tincture was then adjusted so that 100 cc. of it would contain 25 mg. of the alkaloids of stramonium. After adjustment, the physical properties were determined with the following results:

Specific gravity.....	0.9252
pH value.....	6.17
Color of fresh preparation.....	Medium brown
Odor.....	Slightly tobacco-like
Taste.....	Slightly pungent
Total extractive.....	1.5252 Gm. per 100 cc.

A comparison of the two tinctures was made. The alkaloidal strength of the Tincture made by the cooker method was slightly lower than that made by the official method; however, both tinctures were above the official standard for alkaloidal content. The specific gravities and pH values are within a comparatively close range of each other. The total extractive of the pressure cooker Tincture is less than that made by the official method. Three hours were required to make the Tincture by the cooker process, whereas 30 hours were required to make the Tincture by the official method. It was, therefore, comparing Stramonium Tincture, although it is not as efficient as the official paring Stramonium Tincture, although it is not as efficient as the official method for the extraction of the alkaloids.

## 5. Ginger

Preparation of Ginger Fluidextract U.S.P., XIII (19). This fluidextract was prepared by Process A (5), using a mixture of 9 volumes of alcohol and 1 volume of water as the menstruum. Macerate the drug over night, and percolate at a moderate rate.

The Fluidextract was assayed by the official method (20). "Place 20 cc. of Ginger Fluidextract in a 200 cc. beaker, and evaporate on a water bath until there is no longer any odor of alcohol. Remove the beaker from the bath, and add 50 cc. of ether. Stir the contents of the beaker with a stirring rod to dissolve the soluble resin, and decant the ether through a dry, 9 cm. filter into a tared, 200 cc. beaker. Repeat the extraction two or three times, using 50 cc. portions of ether. Wash the filter with a small amount of ether, and evaporate the combined ether extracts on a water bath until the odor of ether is no longer perceptible. Finally dry in a desiccator over sulfuric acid for 18 hours, and then weigh. The weight of the residue should not be less than 900 mg.

The assay gave 6.6975 Gm. of ether-soluble extractive for 100 cc. of Ginger Fluidextract. The physical properties were determined with the following results:

Specific gravity.....	0.8519
pH value.....	6.5
Color of fresh preparation.....	Deep reddish brown
Odor.....	Spicy
Taste.....	Strongly pungent

Ginger Fluidextract Prepared by the Pressure Cooker Method. The formula used

in the manufacture of this fluidextract is as follows:

Ginger, in fine powder.....	200 Gm.
Alcohol.....	540 cc.
Water.....	60 cc.



The ginger was weighed and placed in the pressure cooker. The alcohol and water were mixed and poured over the drug. The mixture was allowed to macerate for 15 minutes and was then cooked for 10 minutes at 15 pounds pressure. The contents of the cooker was filtered through cotton. Enough of a mixture of 9 volumes of alcohol and 1 volume of water was passed through the filter to measure 170 cc.

The Fluidextract was assayed according to the official method (20). Only 2.829 Gm. of ether-soluble extractive was obtained from 100 cc. of the Fluidextract. The physical properties were determined with the following results:

Specific gravity.....	0.8610
pH value.....	6.67
Color of fresh preparation.....	Deep reddish brown
Odor.....	Spicy
Taste.....	Strongly pungent

Ginger Fluidextract Prepared by the Pressure Cooker Method (Maceration

Procedure). Since the Fluidextract made by the cooker method was unsatisfactory, the following formula was tried:

Ginger, in fine powder.....	200 Gm.
Alcohol.....	540 cc.
Water.....	60 cc.

The ginger was weighed and placed in the pressure cooker. The alcohol and water were mixed and poured over the drug, and the mixture was allowed to macerate over night in the closed cooker. The mixture was then cooked for 5 minutes at 15 pounds pressure. The contents was filtered through cotton. Enough of a mixture of 9 volumes of alcohol and 1 volume of water was passed through the filter to measure 170 cc.

The Fluidextract, when assayed by the official method (15), gave only 2.2540 Gm. of ether-soluble extractive per 100 cc. of the Fluidextract.

In the cases of the Fluidextracts made by the cooker method, the drug

was not exhausted as was the case with the official method. Although the two fluidextracts made by the cooker method were similar in appearance to the Fluidextract made by the official method, they must be considered unsatisfactory because they do not conform to the official standard for ether-soluble extractive -- the yield being too low.

## 6. Ipecac

Preparation of Ipecac Fluidextract, U.S.P., XIII (21). This fluidextract was prepared as follows: "Exhaust 100 Gm. of ipecac, in fine powder, by percolation, using a mixture of 3 volumes of alcohol and 1 volume of water as the menstruum, macerating for 72 hours, and percolating slowly. Reduce the entire percolate to a volume of 100 cc. by evaporation at a temperature not exceeding 60° C., and add 200 cc. of water. Allow the mixture to stand and add 200 cc. of water. Allow the mixture to stand over night, filter, and evaporate the filtrate to a volume of 56.5 cc. To this add 3.5 cc. of hydrochloric acid and 30 cc. of alcohol, mix well, and filter."

This fluidextract was assayed by the official method (21). "Measure accurately 10 cc. of Ipecac Fluidextract, and transfer it to an evaporating dish containing either absorbent paper or asbestos, and dry at a temperature not exceeding 60° C. Transfer the absorbent to a flask containing 100 cc. of peroxide-free ether, measured at 25° C., stopper the flask tightly, shake well, and allow the mixture to stand for 5 minutes. Then add 10 cc. of ammonia T.S., using a portion of the ammonia T.S. to rinse traces of the absorbent from the evaporating dish. Stopper the flask tightly, shake it intermittently during two hours, and allow it to stand over night at a temperature not exceeding 25° C. Again shake the mixture intermittently during 30 minutes, and allow the absorbent to settle at 25° C. Then quickly transfer to a separator exactly 50 cc. of the clear supernatant liquid, representing 5 cc. of the Fluidextract, rinse the measuring vessel with a small volume of peroxide-free ether, and add the rinsing to the solution in the separator. Completely extract the alkaloids from the ether with approx-

imately normal sulfuric acid, preferably using 15 cc. the first time, or sufficient to insure an acid reaction, and 10 cc. for each succeeding extraction, and filtering all extractions through the same filter into a second separator. To the combined acid solutions add about an equal volume of peroxide-free ether, render the mixture alkaline with ammonia T.S., and completely extract with successive portions of peroxide-free ether. Filter each portion of the ether extract into a flask or beaker, and carefully evaporate the combined ether extracts on a steam bath until nearly but not quite dry. Add 5 cc. of peroxide-free ether and exactly 10 cc. of tenth-normal sulfuric acid, and heat on a steam bath to effect complete solution of the alkaloid and to remove all of the ether. Cool, dilute with 15 cc. of water, and titrate the excess of acid with tenth-normal sodium hydroxide, using methyl red T.S. as the indicator. Each cc. of tenth-normal sulfuric acid is equivalent to 24.0 mg. of the ether-soluble alkaloids of ipecac."

The yield of ether-soluble alkaloids of ipecac was 1.992 Gm. per 100 cc. of the Fluidextract. The physical properties were determined with the following results:

Specific gravity.....	1.0123
pH value.....	0.63
Color of fresh preparation.....	Deep reddish brown
Odor.....	Vine-like
Taste.....	Burning-sour
Total extractive.....	15.2982 Gm. per 100 cc.

Ipecac Fluidextract Prepared by the Pressure Cooker Method. The formula used in the manufacture of this fluidextract is as follows:

Ipecac, in fine powder.....	100 Gm.
Alcohol.....	300 cc.
Water.....	100 cc.

The ipecac was weighed and placed in the pressure cooker. The alcohol and water were mixed and poured over the drug. The mixture was allowed to stand over night and was then cooked for 10 minutes at 15 pounds pressure. The contents

of the cooker was filtered through cotton. The filtrate was evaporated to 100 cc., and 200 cc. of water was added to it. The mixture was allowed to stand over night and filtered. The filtrate was then evaporated to 56.5 cc., and 3.5 cc. of hydrochloric acid and 30 cc. of alcohol were added to the evaporated filtrate. The finished product was mixed well.

This fluidextract was assayed by the official method (21). The results of the assay showed 1.25 Gm. of the ether-soluble alkaloids of ipecac in 100 cc. of the Fluidextract. The physical properties were determined with the following results:

Specific gravity.....	0.9722
pH value.....	0.77
Color of fresh preparation.....	Deep reddish brown
Odor.....	Wine-like
Taste.....	Burning-sour

In comparing the two fluidextracts, the color, odor, and taste were identical. There was only a slight variation in the pH values and the specific gravities, but there was an appreciable difference in alkaloidal content and total extractive. The alkaloidal content of the Fluidextract prepared by the pressure cooker method was only 1.25 Gm. per 100 cc., whereas the official requirement is 1.8 to 2.2 Gm. per 100 cc. Therefore, it must be concluded that the pressure cooker method is unsatisfactory for the preparation of Ipecac Fluidextract.

## 7. Cascara Sagrada

Preparation of Cascara Sagrada Fluidextract, U.S.P., XIII (22), by

Process B. "This fluidextract was prepared by Process B (7). Evaporate the percolate until it measures 800 cc. and when it is cold, gradually add 200 cc. of alcohol and, if necessary, sufficient water to make the product measure 1000 cc. Mix thoroughly."

The U.S.P., XIII, requires no official assay for this preparation.

The physical properties were determined with the following results:

Specific gravity.....	1.0783
pH value.....	5.00
Color of fresh preparation.....	Dark brown
Odor.....	Slightly alcoholic
Taste.....	Very bitter
Total extractive.....	24.0686 Gm. per 100 cc.

Cascara Sagrada Fluidextract Prepared by the Pressure Cooker Method. Since

all previous attempts to prepare fluidextracts by the pressure cooker method have failed, it was decided to try the following formula:

Cascara Sagrada, in very coarse powder.....	100 Gm.
Boiling water, a sufficient quantity	
Alcohol.....	20 cc.

The cascara sagrada was placed in the pressure cooker, and 400 cc. of boiling water was poured over the drug. The mixture was allowed to macerate for 15 minutes and was cooked for 10 minutes at 15 pounds pressure. The contents of the cooker was filtered through cotton. Boiling water was passed through the drug until it was exhausted. The filtrate was evaporated to 80 cc. on a water bath and allowed to stand in a stoppered container for several days. The clear liquid was decanted and the remainder was filtered into the decanted liquid. The residue on the filter was washed with a sufficient quantity of a

mixture of alcohol and water to make the Fluidextract measure 100 cc. and contain the required proportion of alcohol. Mix thoroughly.

The physical properties were determined with the following results:

Specific gravity.....	1.0825
pH value.....	4.95
Color of the fresh preparation.....	Dark brown
Odor.....	Alcoholic and pungent
Taste.....	Very bitter
Total extractive.....	23.5982 Gm. per 100 cc.

Since the U.S.P., XIII, provides no official assay for these fluid-extracts, a comparison must be made with respect to their physical properties. With respect to specific gravity, pH value, odor, taste, and color, the two are practically identical. Their total extractive contents are almost alike. Two hours less time is required to make the Fluidextract by the pressure cooker method.

It should be pointed out that this was the first instance in this series of experiments, using the pressure cooker method of the preparation of fluidextracts, that the drug was exhausted. In view of the closeness of the values obtained for the total extractive and the similarity in the physical properties of the two fluidextracts, it is concluded that this modified pressure cooker method is a satisfactory substitute for the official method in the preparation of Cascara Sagrada Fluidextract, and that it has an advantage over the official method in that time is saved.

## 8. Wild Cherry

Preparation of Wild Cherry Syrup, U.S.P., XIII (23). The following formula was used to make the Wild Cherry Syrup:

Wild Cherry, in coarse powder.....	30 Gm.
Glycerin.....	30 cc.
Sucrose.....	135 Gm.
Alcohol.....	4 cc.
Water, a sufficient quantity, To make.....	200 cc.

"Moisten the wild cherry with 20 cc. of water, pack in a cylindrical percolator, and pour sufficient water upon it to saturate the powder and leave a water stratum above it. Close the lower orifice, cover the percolator, and macerate the drug for 1 hour. Then allow the percolation to proceed rapidly, and collect 80 cc. of percolate, using additional water as the menstruum. Filter the percolate, add the sucrose and dissolve it by agitation, then add the glycerin, the alcohol, and sufficient water to make the finished product measure 200 cc."

The physical properties of the Syrup were determined with the following results:

Specific gravity.....	1.286
pH value.....	4.65
Color of fresh preparation.....	Medium red
Odor.....	Cherry-like
Taste.....	sweet

Wild Cherry Syrup Prepared by the Pressure Cooker Method. This syrup was made from the following formula:

Wild Cherry, in coarse powder.....	30 Gm.
Glycerin.....	30 cc.
Sucrose.....	135 Gm.
Alcohol.....	4 cc.
Water, a sufficient quantity, To make.....	200 cc.



The wild cherry was placed in the cooker, and 130 cc. of water was poured over the drug. The mixture was allowed to macerate for 15 minutes and then was cooked for 5 minutes at 15 pounds pressure. The contents of the cooker was filtered through cotton. Sufficient water was passed through the filter to make the total volume of the filtrate measure 80 cc. The filtrate was filtered until clear and added to the sucrose, which was dissolved by agitation. Then the glycerin, alcohol, and sufficient water were added to make the final product measure 200 cc.

The physical properties of the Syrup were determined with the following results:

Specific gravity.....	1.2820
pH value.....	4.65
Color of the fresh preparation.....	Lighter red than the official Syrup.
Odor.....	Cherry-like
Taste.....	Sweet

Wild cherry bark contains the glucoside *α*-mandelonitrile, and a thermolabile enzyme, emulsin (24). When the drug is moistened, the glucoside and the enzyme react to produce hydrocyanic acid, benzaldehyde, and glucose. These products are thought to be the active constituents of wild cherry bark. Army (25) states that the ferment, emulsin, is rendered inactive when treated with hot water, preventing the formation of hydrocyanic acid. Hence, all official preparations of the bark are directed to be made with cold solvents.

In the case of the Syrup made by the pressure cooker method, according to the literature, no hydrocyanic acid should be present in it, whereas hydrocyanic acid should be present in the official Syrup. However, when the pH values of the two syrups were compared, they were found to be identical, proving that the amount of acidity is the same in both cases. Evidently, the short period of maceration previous to cooking is sufficient time for enzyme action to take place with the normal yield of hydrocyanic acid. A comparison

of their specific gravities shows a difference of only 4 in the third decimal place. Their odors and tastes are similar. The color of the official preparation is only slightly darker than the preparation made with the pressure cooker.

On the basis of their physical properties, it was concluded that the Syrap made by the pressure cooker method is entirely satisfactory, and that approximately one hour in time is saved as compared with that consumed by the official method of preparation.

## 9. Digitalis

Digitalis Tincture Prepared by the Pressure Cooker Method. The following formula was used to make this tincture:

Digitalis, in fine powder.....	49.6 Gm.
Alcohol.....	400.0 cc.
Water.....	100.0 cc.

At first glance the amount of digitalis to be used might be questioned. The official formula calls for 40 Gm. of the drug to 400 cc. of the finished Tincture. However, 49.6 Gm. of powdered digitalis were used, because 1 Gm. as stated on the label was equivalent to only 8.05 cat units.

The digitalis was weighed and placed in the pressure cooker. The alcohol and water were mixed and poured over the drug, and the mixture was allowed to macerate over night. The mixture was cooked for 5 minutes at 15 pounds pressure and filtered through cotton. A sufficient quantity of a mixture of 4 volumes of alcohol and 1 volume of water was passed through the filter to make the final product measure 400 cc.

Assay of Digitalis Tincture. The Tincture was assayed by the over-night frog method (26).

(a) Preparation of the U.S.P., XIII, Digitalis Reference Standard (27).

Weigh the contents of one ampule of Digitalis Reference Standard, and transfer to a dry, hard-glass, glass-stoppered container of at least 50 cc. capacity. Add sufficient menstruum consisting of 4 parts of alcohol and 1 part of water, so that the total volume of menstruum added corresponds to 10 cc. for each Gm. of powder. Shake the mixture for 24 hours at 25° C. by mechanical means. Immediately thereafter, centrifuge the mixture and decant into a dry, hard-glass bottle having a tight closure.

(b) Preparation of the Crude Drug Macerate. Place 4 Gm. of powdered digitalis, used in the preparation of the Tincture, in a glass stoppered flask. Add a sufficient quantity of menstruum consisting of 4 parts of alcohol and 1 part of water to the drug, so that the total volume of menstruum added corresponds to 10 cc. for each Gm. of drug. Shake the mixture for 24 hours at 25° C. by mechanical means and centrifuge. Decant into a dry, hard glass bottle having a tight closure.

(c) Preparation of the Dilutions. After numerous orienting assays, the following dilutions were made:

Standard - Dilute 4.8 cc. of the standard Tincture to 20 cc. with distilled water.

Pressure Cooker Tincture - Dilute 6.5 cc. of this tincture to 20 cc. with distilled water.

Crude Drug Macerate - Dilute 6.5 cc. of this macerate to 20 cc. with distilled water.

(d) Injection Procedure. Three groups of 15 frogs each were used in this assay. Each frog of the first group received an injection of .02 cc. of the standard dilution per Gm. body weight. Each frog of the second group received .02 cc. of the cooker tincture dilution per Gm. body weight. Each frog of the third group received .02 cc. of the crude drug macerate dilution per Gm. body weight. All injections were made into the abdominal lymph sac. The frogs were placed in a water bath at 20° C.  $\pm$  1° C. and left until the following day, when the number of dead frogs in each group was counted. From the percentage mortality and the characteristic curve for frogs, the curve number was determined.

The arbitrarily selected curve numbers are obtained from Table I, assuming a dose value of 4.0 for 50% mortality, and calculating corresponding curve numbers to all possible percentage mortalities when 15 frogs are

employed for the standard and unknown in a test. The numbers have been calculated from the regression coefficient, 13.1, for digitalis (28).

Table No. I. - The Relationship between Percentage Mortality and the Curve Number for Digitalis Tincture

No. Dead	% Mortality	Curve Number
1	6.67	3.10
2	13.34	3.31
3	20.00	3.47
4	26.67	3.60
5	33.34	3.72
6	40.00	3.83
7	46.67	3.95
8	53.34	4.08
9	60.00	4.20
10	66.67	4.35
11	73.34	4.47
12	80.00	4.66
13	86.67	4.88
14	93.34	5.21
15	100.00	-----

(e) Data Sheet for the Assay.Sample: Digitalis Tincture (Pressure Cooker Method).Dilution: 6.5 cc. to 20 cc., Dose: .0065 cc./Gm.  
Mortality: 10/15, % Mortality: 66.67, Curve No. 4.35Standard: U.S.P., XIII, Digitalis Reference StandardDilution: 2.4 cc. to 10 cc., Dose: .0048 cc./Gm.  
Mortality: 9/15, % Mortality: 60.0, Curve No. 4.20Result:

$$100 \text{ cc. of the sample} = \frac{4.35}{4.20} \times \frac{.0048}{.0065} \times 100 = 76.5 \text{ cc. of the standard Tincture.}$$
Crude Drug Macerate: Macerate of Digitalis PowderDilution: 6.5 cc. to 20 cc., Dose: .0065 cc./Gm.  
Mortality: 4/15, % Mortality: 26.67, Curve No. 3.60Result:

$$100 \text{ cc. of the crude macerate} = \frac{3.60}{4.20} \times \frac{.0048}{.0065} \times 100 = 63.3 \text{ cc. of the standard Tincture.}$$

The above result only applies if 40 Gm. of powdered digitalis is used per 400 cc. of the finished Tincture. Since 49.6 Gm. of the powdered digitalis is used per 400 cc. of the final Tincture, the calculation should be as follows:

$$\frac{40}{63.3} = \frac{49.6}{x} \quad x = 78.5 \text{ cc.}$$

Therefore, 100 cc. of the crude macerate is equivalent to 78.5 cc. of the standard Tincture.

Comparison of the Sample and the Crude Drug Macerate.

$$\frac{76.5}{78.5} \times 100 = 97.45 \%$$

extraction of the glycosides of digitalis. Thus, the Tincture prepared by the pressure cooker method is 97.45 % as potent as the macerate made from the crude drug.

The physical properties of the Tincture were determined with the following results:

Specific gravity.....	0.8610
pH value.....	5.69
Color of fresh preparation.....	Dark brownish green
Odor.....	Tobacco-like
Taste.....	Slightly bitter

The above results indicate that Digitalis Tincture made by the pressure cooker method compares favorably in potency with the standard made from the crude drug. Practically complete extraction of the glycosides of digitalis was accomplished in the preparation of the Tincture by this method.

Table No. II. - Physical Properties - Color, Odor, Taste and Changes on Storage of the Preparations Made

Preparation	Color		Odor		Taste		Changes on Storage	
	Official Method	Cooker Method	Official Method	Cooker Method	Official Method	Cooker Method	Official Method	Cooker Method
<b>Nux Vomica Tincture</b>	Orange	Yellow	Wine-like	Wine-like	Very bitter	Very bitter	From orange to reddish orange	From yellow to amber
<b>Belladonna Tincture</b>	Dark greenish brown	Dark greenish brown	Tobacco-like	Tobacco-like	Alcoholic	Alcoholic	No apparent change	No apparent change
<b>Hyoscyamus Tincture</b>	Dark greenish brown	Dark greenish brown	Tobacco-like	Tobacco-like	Slightly pungent	Slightly pungent	No apparent change	No apparent change
<b>Stramonium Tincture</b>	Dark greenish brown	Medium brown	Slightly tobacco-like	Slightly tobacco-like	Pungent	Slightly pungent	Slight precipitate	No apparent change
<b>Ginger Fluidextract</b>	Deep reddish brown	Deep reddish brown	Spicy	Spicy	Strongly pungent	Strongly pungent	No apparent change	No apparent change
<b>Ipecac Fluidextract</b>	Deep reddish brown	Deep reddish brown	Wine-like	Wine-like	Burning-sour	Burning-sour	No apparent change	No apparent change
<b>Cascara Sagrada Fluidextract</b>	Dark brown	Dark brown	Slightly alcoholic	Alcoholic and pungent	Very bitter	Very bitter	Slight precipitate	Slight precipitate
<b>Wild Cherry Syrup</b>	Medium red	Light red	Cherry-like	Cherry-like	Sweet	Sweet	No apparent change	No apparent change
<b>Digitalis Tincture</b>		Dark brownish green		Tobacco-like		Slightly bitter		Slight precipitate



Table No. III. - Specific Gravities of the Preparations Made

Preparation	Specific Gravity at 25° C.	
	Official Method	Cooker Method
Nux Vomica Tincture	0.8872	0.8999
Belladonna Tincture	0.8840	0.8950
Hyoscyamus Tincture	0.8880	0.8992
Stramonium Tincture	0.8853	0.9252
Ginger Fluidextract	0.8549	0.8610
Ipecac Fluidextract	1.0123	0.9722
Cascara Sagrada Fluidextract	1.0783	1.0825
Wild Cherry Syrup	1.2859	1.2820
Digitalis Tincture		0.8610

Table No. IV. - pH Value of the Preparations

Preparation	pH Value	
	Official Method	Cooker Method
Nux Vomica Tincture	1.70	5.15
Belladonna Tincture	6.27	6.32
Hyoscyamus Tincture	6.05	6.12
Stramonium Tincture	6.17	6.17
Ginger Fluidextract	6.50	6.67
Ipecac Fluidextract	0.63	0.77
Cascara Sagrada Fluidextract	5.00	4.95
Wild Cherry Syrup	4.65	4.65
Digitalis Tincture		5.69

Table No. V. - Total Extractive and Alkaloidal Content of the Preparations

Preparation	Total Extractive Official Method Gm./100 cc.	Alkaloids Official Method Gm./100 cc.	Total Extractive Cooker Method Gm./100 cc.	Alkaloids Cooker Method Gm./100 cc.
Nux Vomica Tincture No. 1	1.3776	Strychnine 0.1252 0.1241		
Nux Vomica Tincture No. 2				Strychnine 0.1133
Nux Vomica Tincture No. 3				Strychnine 0.1167
Nux Vomica Tincture No. 4				Strychnine 0.855
Nux Vomica Tincture No. 5			1.3050	Strychnine 0.1110 0.1101
Nux Vomica Fluidextract		Strychnine 1.264 1.241		Strychnine 0.3912 0.3922
Belladonna Tincture	1.1394	0.0503 0.0499	0.9992	0.0503 0.0499
Hyoscyamus Tincture	1.7896	0.00495 0.00488	1.4850	0.00519 0.00526
Stramonium Tincture	1.5686	0.0427 0.0425	1.5282	0.0361 0.0353
Ginger Fluidextract	6.6975 ether-soluble		2.829 ether-soluble	
Ipecac Fluidextract	15.2982	1.992	10.3712	1.250
Cascara Sagrada Fluidextract	24.0886		23.5982	

## DISCUSSION

For the purpose of these experiments the drugs used were limited to those, the tinctures and fluidextracts of which are official, so that the preparations made by the pressure cooker method could be compared with similar preparations made by the official methods. The number of drugs was further restricted to those which contained an active principle or principles for which there was an official assay provided. Wild cherry bark and cascara sagrada are exceptions to this rule, and were selected for other reasons as will be described later. In addition to the foregoing, the drugs worked with, were selected, because they are representative of different groups of drugs containing constituents which determine, to a large extent, the selection of the method to be used in extraction.

With regard to the results of the experiments heretofore described, it may be said, in general, that there is very little difference in the physical appearance of the preparations made by the pressure cooker method as compared with those made by the official methods. There is very little difference in color, odor, and taste, except in the case of the two Nux Vomica Tinctures. The Tincture prepared by the official method was orange colored, whereas that prepared by the pressure cooker method was pale yellow, evidently due to the fact that there is less total extractive in the Tincture made by this method than in that made by the official process.

The pH values and specific gravities of the preparations made from the same drug, checked very closely. Again there is an exception to this general statement insofar as the pH values are concerned. The fact that the Nux Vomica Tincture prepared by the official method showed a pH value of 1.70, whereas that prepared by the cooker method showed a pH value of 5.15, is

readily understandable, when it is recalled that hydrochloric acid was added to the menstruum in the preparation of the Tincture by the official method, whereas acetic acid was used in the preparation of the Tincture by the cooker method.

In those cases where the pressure cooker method yielded a product equally as good in quality as that yielded by the official methods of extraction, the alkaloidal contents of the individual preparations were very close to or above those found for similar preparations made by the official methods. This was found to be the case regardless of whether the drugs were representative of the groups containing tannin, resins, or other extractive material.

The total extractive found for the preparations made by the pressure cooker method was noticeably less than that found in the preparations made by the official methods, except in the cases of the Nux Vomica Tinctures and the Stramonium Tinctures. In the Nux Vomica Tinctures the difference was approximately 5%. In the case of the two Stramonium Tinctures the difference was only about 2.5%. The fact that the amount of extractive obtained from preparations made by the pressure cooker method is, as a general rule, noticeably less than that obtained from preparations made by official methods, is to be explained on the basis of the slow rate of solubility of some of the constituents of the extractive or on the assumption that some of the constituents, such as albumin and proteins, which are present in plants and which are ordinarily found in the extractive, are coagulated and rendered insoluble by the application of heat, which is required in the pressure cooker method. The fact that there is less extractive obtained by the pressure cooker method, is one of the important advantages of using this method, since it can be said, as a general rule, that the less the extractive content of a preparation, the more stable it is likely to be.

In those cases where the pressure cooker method gave unsatisfactory results, as for instance, in the preparation of fluidextracts, it was believed to be due to the comparatively small amount of menstruum per weight of drug used in their preparation as compared to the amount of menstruum used in the preparation of tinctures. Thus, the quantity of menstruum used, was not sufficient to exhaust the drug of its alkaloids. A way to overcome this apparent deficiency of the pressure cooker method would be to use more menstruum, but in so doing, it would require adjustment by evaporation of the volume of the resulting fluidextract to that prescribed. This would eliminate the principal advantage of the use of this method, which is the saving of time.

From the standpoint of the advantage to be gained in making the preparations used in these experiments, the pressure cooker method was found to effect a very considerable saving in time, in those cases in which it could be considered a satisfactory substitute or improvement over the official method. The saving in time of 1 to 28 hours was effected in making the preparations described herein by the pressure cooker method as compared with the time consumed in making these preparations by the official methods. The least saving in time, 1 hour, was obtained in the preparation of Wild Cherry Syrup, because the U.S.P., XIII, requires that the wild cherry be macerated for only 1 hour. The greatest saving in time, 28 hours, was obtained in the preparation of Nux Vomica Tincture, because the official formula requires the drug to be macerated for 24 hours, and approximately 30 hours are necessary to complete the preparation, whereas the Tincture made by the pressure cooker method requires only 2 hours for its preparation.

From the results obtained, it is believed an equal saving of time could be effected for other official preparations, which are made by extraction.

## CONCLUSIONS

1. The pressure cooker method was found to be very efficient in the preparation of the tinctures of the Solanaceae family, especially belladonna and hyoscyamus.
2. A satisfactory modification of the official formula for making Nux Vomica Tincture by the pressure cooker method, was devised. It differs from the N.F., VIII, formula, in that the menstruum used contains acetic acid instead of hydrochloric acid.
3. Digitalis Tincture of satisfactory quality was made by the pressure cooker method. The over-night frog assay showed that almost complete extraction of the glycosides of digitalis was accomplished by this method.
4. Practically all of the tinctures made by the pressure cooker method conform to the official standards, indicating that this method is satisfactory for the preparation of tinctures. The lack of conformity to official standards in the cases of the fluidextracts prepared shows that this method is not satisfactory for the preparation of fluidextracts, when the official menstruum is used in quantities prescribed by the official methods. It is believed, however, that modifications of the official formulae for making fluidextracts by the pressure cooker method can be devised, which will yield preparations of satisfactory quality, but that the amount of time saved over that required for making these preparations by the official methods, will be considerably less than in the case of tinctures.
5. In the cases where the pressure cooker method is satisfactory, it has many advantages over the official extraction methods. The time consumed in making these classes of preparations by the pressure cooker method is, in

general, approximately 1/10 to 1/15 as much as that required to produce similar preparations by the official methods. Also, the time-consuming procedure of packing the percolator and regulating the flow of the percolate is eliminated, if the pressure cooker method is used.

6. The results obtained in these preliminary experiments indicate that there are possibilities in the use of the pressure cooker for improving the drug extraction methods of the official compendia, particularly with reference to the preparation of tinctures and fluidextracts, and to a lesser degree the preparation of other galenicals.

## REFERENCES

1. May, Earl P., The Canning Clan, p. 26, Macmillan, New York, N. Y., 1937.
2. Anon., The Index, 13 (1933) 116
3. Carroll, Leone R., Pressure Cookery, p. 13, M. Barrows and Company, Inc., New York, N. Y., 1947.
4. U.S.P., 13th Rev. (1947) p. 708.  
N.F., 8th Edit. (1946) p. 758.
5. U.S.P., 13th Rev. (1947) p. 654.  
N.F., 8th Edit. (1946) p. 718.
6. U.S.P., 13th Rev. (1947) p. 655.  
N.F., 8th Edit. (1946) p. 718.
7. U.S.P., 13th Rev. (1947) p. 656.  
N.F., 8th Edit. (1946) p. 719.
8. U.S.P., 13th Rev. (1947) p. 714
9. N.F., 8th Edit. (1946) p. 363.
10. U.S.P., 10th Rev. (1926) p. 400.
11. N.F., 8th Edit. (1946) p. 362.
12. Ibid., p. 359.
13. U.S.P., 13th Rev. (1947) p. 66.
14. Ibid., p. 67.
15. Ibid., p. 262.
16. Ibid., p. 263.
17. Ibid., p. 519.
18. Ibid., p. 520.
19. Ibid., p. 236.
20. Ibid., p. 237.
21. Ibid., p. 279.



## REFERENCES (Continued)

22. U.S.P., 13th Rev. (1947) p. 115.
23. Ibid., p. 604.
24. Brecht, Edward A., American Pharmacy, p. 233,  
J. B. Lippincott Company, Philadelphia, Pa., 1945, Vol. I.
25. Army, H.V., and Fischelis, R.P., Principles of Pharmacy, p. 795,  
W. B. Saunders Company, Philadelphia, Pa., 1937, 4th Edit.
26. Chapman, C.W., and Morrell, C.A.,  
J. Pharmacol. Exptl. Therap., 46 (1932) 229.
27. U.S.P., 13th Rev. (1947) p. 173.
28. Allmark, M.C., and Morrell, C.A.,  
J. Amer. Pharna. Ass., Sci. Edit., 30 (1941) 1.