

KINO, GAMBIR AND CATECHU.*

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The preparation of the monographs of kino and gambir for the tenth revision of the U. S. Pharmacopœia has led to a study of these astringent substances and their comparison with black catechu. Our studies are not complete but we present herewith the data obtained to date.

The investigation has developed along the lines indicated by the following questions:

1. Do these astringent drugs deteriorate upon aging?
2. Is the solubility in water, alcohol or hydroalcohol a suitable test for the determination of the quality of these drugs?
3. Are there any tests of identity for these drugs?
4. Why is gambir preferable to black catechu as an astringent drug?

As a preliminary thought, let us assume that the therapeutic value of the three drugs lies in their astringency and that their active principles are the astringent substances present in them.

Kino-tannic acid is the name applied to the water-soluble astringent substance or substances of kino, and catechu-tannic acid to the similar substances of catechu and gambir. These tannic acids belong to the group of non-glucosidal tannins that form a green coloration with ferric salts, a precipitate with bromine water, produce catechol upon prolonged heating, phlobaphenes upon treatment with dilute acids and protocatechuic acid when fused with potassium hydroxide. Hence, they differ markedly from the gallo-tannins, that are glucosidal, form a blue-black coloration with ferric salts, no precipitate with bromine water, pyrogallol upon volatilization and gallic or ellagic acid upon treatment with dilute acids or when fused with alkalis.

Along with catechu-tannic acid, there is present in catechu, for instance, catechin and probably several anhydrides of catechin. To catechin, which is obtainable in white silky crystals, the formula $C_{15}H_{18}O_8$ is usually assigned. Allen ("Commercial Organic Analysis," 4th ed.) suggests the following series of anhydrides:

Catechin $C_{38}H_{36}O_{16}$ ($2C_{19}H_{18}O_8$)	Dianhydride $C_{38}H_{32}O_{14}$
Catechu-tannic acid $C_{88}H_{84}O_{48}$	Tri-anhydride $C_{38}H_{30}O_{13}$
Catechuretine $C_{38}H_{28}O_{12}$	

Catechin possesses no acid properties, does not precipitate gelatin or the alkaloids as do the tannins, is readily soluble in alcohol, ether and boiling water but only slightly so in cold water. When heated, catechin forms catechu-tannic acid.

Catechu-tannic acid, a dark reddish brown powder, though its color may be due to the presence of impurities, precipitates gelatin and the alkaloids, is readily soluble in cold water, alcohol and ethyl acetate but insoluble in ether. When heated, it forms catechal and with dilute acids forms water-insoluble phlobaphenes.

Allen states that phlobaphenes are red or brown amorphous substances which are but slightly soluble or sometimes insoluble in either cold or boiling water or in weak acid solutions or in ether but are soluble in dilute solutions of the alkalies and in alcohol. The greater the anhydration of the phlobaphenes the less the solubility in water. Those that are water-soluble precipitate gelatin, combine with hide

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to form leather and behave with many reagents like their respective tannins.

Kino, correspondingly, is said to possess:

Kinoin	$C_{28}H_{24}O_{12}$ ($2C_{14}H_{12}O_6$)	Kino red	$C_{28}H_{22}O_{11}$
Kino-tannic acid	$C_{28}H_{21}O_{11}$	Dianhydride	$C_{28}H_{20}O_{10}$

There is much confusion regarding the formulas of these substances. Kino-tannic acid has not been isolated in a positively pure form. Yet that a series of anhydrides exists seems to be well established.

Kinoin has been obtained in colorless crystals. It does not precipitate gelatin, dissolves readily in boiling water, in alcohol and in ether and but slightly in cold water.

The proportion of these substances present in the drugs under discussion varies so widely that it is difficult to correlate the reports of various investigators. Allen states:

Catechu contains tannin 45-55%, catechin 30-40%
 Gambir contains tannin 36-40%, catechin 20-30%
 Kino contains tannin 75%, kinoin in small amount

The data we have obtained regarding the solubility of these three drugs are compared with the statements made in a number of standard texts; *viz.*:

"Pharmacopœia of the United States IX" (U. S. P.)
 "British Pharmacopœia, 1914" (B. P.)
 "Deutsches Arzneibuch," 5th ed. (G. P.)
 "National Standard Dispensatory, 3rd ed." (N. D.)
 "Kraemer's Pharmacognosy," 2nd ed. (Kr.)
 "Greenish's Pharmacognosy" (Gr.)
 "Flückiger and Hanbury's Pharmacographia" (Fl.)

The work of Professor R. L. Newcomb (New.) on moisture and ash published in the U. S. P. X Revision Bulletins is also quoted.

As indicated by the following list we have examined fifteen specimens of kino, eleven of gambir and eleven of black catechu. The specimens are numbered according to their age, the more recent bearing the larger numbers. However, with some of the older specimens it was impossible to determine their exact age and even with recent purchases we have no way of ascertaining the age back of the date of purchase, but in every case the specimen is at least as old as the year indicated.

Kino.	Gambir.	Catechu.
1—Yo. 1922	1—Yo. 1922	1—Yo. 1922
2—L. & F. 1921	2—L. & F. 1921	2—L. & F. 1921
3—L. & F. 1921	3—L. & F. 1921	3—Chaw. 1921
4—New. 1921	4—L. & F. 1918	4—L. & F. 1919
5—L. & F. 1920	5—L. & F. 1915	5—U. of I. 1910
6—L. & F. 1917	6—L. & F. 1914	6—P. D. & Co. 1903
7—P. V. & Co. 1917	7—P. V. & Co. 1914	7—L. & F. 1900
8—L. & F. 1915	8—P. D. & Co. 1903	8—E. L. & Co. 1900
9—Go. 1910	9—E. L. & Co. 1900	9—Go. 1900
10—Go. 1910	10—L. & F. 1922	10—G. L. & Co. 1893
11—P. D. & Co. 1903	11—F. M. & Co. 1922	11—N. W. U. 1893
12—U. of I. 1900		
13—U. of I. 1900		
14—E. L. & Co. 1900		
15—G. L. & Co. 1893		

COMMENTS.

Under Kino, Sample 10 was in angular pieces up to a centimeter across, rather dull in appearance and resembling black catechu fairly uniformly broken. Sample 12 was in powdered form and at least 22 years old in this form. Sample 13 was very finely granular and dull in appearance.

Under Gambir, Samples 7, 8 and 11 were the soft variety of gambir which had become dried into irregular-shaped, blackish masses. All other samples were brown cube gambir. Samples 10 and 11 were added after some experimental work had been done and hence are not in proper chronological order.

Kino.			ASH. Gambir.			Catechu.		
U. S. P.—not more than 3%.			U. S. P.—not more than 9%.			B. P.—not more than 5%.		
B. P.—not more than 2.5%.			B. P.—not more than 5%.			Powd.—not more than 8%.		
Fl.—1.3%.			Powd.—not more than 8%.			G. P.—not more than 6%.		
N. D.—1% to 2.5%.			Gr.—5%.			Kr.—5%.		
			Fl.—2.6%.			Gr.—2% to 3%.		
			N. D.—not more than 6%.			N. D.—5%.		
New.	Total.	Ac. insol.	New.	Total.	Ac. insol.	New.	Total.	Ac. insol.
1	2.56%	0.50%	1	5.74%	2.12%	1	6.76%	0.00%
2	6.23	0.14	2	5.49	0.91	2	8.53	0.11
3	6.25	0.14	3	7.79	2.63	3	8.91	0.28
4	6.76	0.23	4	6.91	1.06	4	9.38	0.00
5	8.14	0.09						
E. N. G.			E. N. G.			E. N. G.		
1	1.1%	12 6.5	1	2.8%	0.2%	1	9.3%	0.94%
2	5.4	13 5.4	2	4.3	0.4	2	5.1	0.9
3	4.8	14 1.0	3	4.1	0.4	3	9.7	0.7
4	5.6	15 1.5	4	4.5	0.4	4	7.5	1.2
5	2.2		5	3.2	0.2	5
6	5.1		6	4.1	0.2	6	8.6	2.1
7	6.0		7	7.0	0.2	7	7.5	1.5
8	1.6		8	8	8.0	0.5
9	1.5		9	9	6.5	0.9
10	1.5					10	12.4	0.8
11	1.9					11	14.0	0.6

COMMENTS.

It is to be noted that according to Newcomb the ash of kino frequently exceeds the 2.5% limit of the B. P. and even the 3% limit of U. S. P. IX. Our results indicate in 7 out of 15 specimens an ash greater than 3%. In all cases the acid-insoluble ash is less than 1%. The ash appears to be mostly soluble in boiling water but not in alcohol.

The ash of gambir in none of Newcomb's 4 samples nor in any of our 7 samples equaled the 9% limit of U. S. P. IX but in several instances exceeded the 5% limit of the B. P., though the B. P. does permit 8% of ash in powdered gambir. George E. Éwe¹ suggests 8% as the ash limit of gambir. This appears to be sufficiently liberal.

The ash of catechu rises notably above the 5% limit of the B. P. In all of Newcomb's 4 samples and in the 10 samples we report upon the ash exceeds 5%, rising in one instance to 14%. However, the acid-insoluble ash in every case is low.

¹ JOUR. A. PH. A., 1920, pp. 309-10.

Kino.	MOISTURE. Gambir.	Catechu.
U. S. P.—not more than 12%.	Gr.—9% to 11%.	Gr.—12% to 15%.
N. D.—13% to 15%.	New.—4% to 9% at 150° F.	
New.—5% to 7.45% at 150° F.		
E. N. G.—at 102° C.		
1—13.5%	1— 9.8%	1—10.4%
2— 8.2	2— 8.5	2— 9.5
3—10.8	3— 8.8	3— 9.9
4—11.2	4— 8.4	4— 8.67
5—10.7	5— 9.1	5— ..
6— 9.1	6— 9.2	6—11.6
7— 9.27	7—13.2	7—10.0
8—12.4	8— ..	8— 8.8
9—12.8	9— ..	9—10.85
10—12.4		10— 9.23
11—11.2		11—10.6
12—11.18		
13—10.98		
14—11.2		
15—13.0		

COMMENTS.

The 12% moisture limit of the U. S. P. for kino is none too liberal for the specimens we report upon. Of the 15 samples 5 have moisture slightly exceeding 12%.

Greenish states that gambir contains 9 to 11% of moisture while black catechu contains 12 to 15%. We noted no difference in the average moisture content of the two drugs.

SOLUBILITY IN HOT WATER.

Kino.			Gambir.			Catechu.			
U. S. P.—not less than 40%.			B. P.—almost entirely.			B. P.—almost entirely.			
B. P.—not less than 75%.			Gr.—almost entirely.			Fl.—completely.			
Fl.—almost entirely.			N. D.—a turbid solution.			Kr.—almost entirely.			
Gr.—more than 80-90%.						G. P.—insol. res. not more than 15%.			
E. N. G.									
	A. I. R.	Sol.	A. A. E.	A. I. R.	Sol.	A. A. E.	A. I. R.	Sol.	A. A. E.
1	3.2	96.8	83.8	10.6	89.4	76.5	0.5	99.5	88.0
2	0.6	99.4	90.8	10.5	89.5	80.8	0.5	99.5	86.5
3	1.0	99.0	86.5	13.7	86.3	71.0	0.7	99.3	92.4
4	0.5	99.5	86.8	10.6	89.4	81.2	4.5	95.5	85.5
5	10.7	89.3	80.7	10.6	89.4	75.0	7.2	92.8	80.0
6	0.5	99.5	87.9	10.6	89.4	76.8	11.3	88.7	75.5
7	1.1	98.9	85.6	39.7	60.3	49.2	17.6	82.4	74.0
8	20.4	79.6	67.4	14.3	85.7	79.0	12.4	87.6	75.0
9	71.8	28.2	16.1	16.4	83.6	...	18.5	81.5	69.0
10	40.4	59.6	47.5	2.8	97.2	88.8	13.9	86.1	79.5
11	53.7	46.3	33.5	15.0	85.0	74.0	14.3	85.7	74.4
12	61.9	38.1	25.0						
13	60.6	39.4	27.2						
14	55.5	44.5	40.0						
15	55.0	45.0	33.4						

A. I. R. = percentage of anhydrous insoluble residue.

Sol. = percentage solubility in hot water (approximately 100° C.).

A. A. E. = percentage of anhydrous aqueous extractive at 100° C.

COMMENTS.

The solubility in hot water and the aqueous extract at 100° C. was determined as follows:

Macerate 1 Gm. of the powdered drug (not coarser than No. 40) in about 50 cc. of boiling water in a suitable flask and maintain at nearly 100° C. in a water-bath with frequent shaking or stirring for 2 hours. Filter into a weighed filter in suitable apparatus in a water-bath maintained at nearly 100° C. Wash the flask with boiling water to remove all the residue into the filter and add sufficient boiling water through the filter to make 100 cc. of filtrate. Dry the residue on the filter to constant weight. The difference obtained by deducting the weight of the anhydrous insoluble residue from the weight of powdered drug taken, expressed in percentage, gives the solubility of the drug in hot water.

Evaporate on a water-bath in a suitable tared dish, an aliquot part of the clear, hot filtrate to a residue and dry the same at 102° C. to constant weight. The weight of the dried residue expressed in percentage gives the anhydrous hot water extractive.

It would appear from the data submitted that the minimum limit set by the U. S. P. for kino of 40% soluble in hot water is very much too low. Even the limit of 75% set by the B. P. is much too low for a reasonably recent kino. The first 7 specimens that we examined were mostly 1 and 2 years old though some were 5 or 6 years old and all are 90% or more soluble in boiling water, while the last 8 specimens are all 8 years or more, even up to 25 or 30 years old, and all fall away below 90% solubility. We are convinced that no kino less than 90% soluble in boiling water is suitable for medicinal use.

The anhydrous aqueous extract plus the anhydrous insoluble residue plus the moisture should equal 100%. We could seldom get these figures exact, but frequently quite close. The anhydrous hot water extract as a constant has an advantage over the solubility determination in that it is not influenced by moisture in the drug. A standard of 80 per cent. of hot water extractive for kino would insure a good quality of drug.

Gambir in boiling water gives a more or less turbid mixture which results in a considerable residue upon filtration. Furthermore, filtration frequently is slow and difficult. Aging the gambir seems to make no difference in its solubility. The soft varieties of gambir, when dried, were somewhat less soluble than the cube gambir; 75 per cent. of anhydrous hot-water extractive would insure a good quality of drug.

Catechu, like kino, is very soluble in boiling water when not aged and of about the same solubility as gambir when aged. The filtrate, upon cooling, usually becomes turbid. It would appear as though a catechu suitable for medicinal use should be not less than 85% soluble in boiling water and 75 per cent. of anhydrous hot water extractive would be a very fair standard for the drug.

Perhaps the criterion frequently employed in the German Pharmacopœia, *viz.*, the anhydrous insoluble residue, is equal in value to either the solubility or the extractive determinations. It requires somewhat less manipulation and calculation than either of the others. An anhydrous insoluble residue after complete extraction with water at 100° C. of not more than 10 per cent. for kino and 15 per cent. for gambir and catechu would insure a good quality of drug.

SOLUBILITY IN COLD WATER.

Kino.			Gambir.			Catechu.			
U. S. P.—partly.			U. S. P.—not less than 65%.			B. P.—partly.			
B. P.—slowly and incompletely.			Kr.—85%.			Fl.—a small portion soluble.			
Gr.—80 to 90%.			N. D.—75%.			Kr.—somewhat.			
Fl.—all but a pale flaky residu.			E. N. G.			E. N. G.			
N. D.—partly, with a flocculent residu.			A. I. R. Sol.			A. I. R. Sol.			
E. N. G.			A. A. E.			A. A. E.			
			A. I. R.			A. I. R.			
			Sol.			Sol.			
			A. A. E.			A. A. E.			
1	32.7	67.3	58.4	20.1	79.9	65.2	6.6	93.4	86.0
2	10.3	89.7	77.2	22.2	77.8	68.0	8.3	91.7	85.6
3	7.5	92.5	82.4	21.2	78.8	64.8	8.4	91.6	82.8
4	0.1	99.9	87.2	24.0	76.0	62.0	17.2	82.8	73.2
5	48.2	51.8	41.2	19.5	80.5	68.8	30.4	69.6	57.6
6	16.8	83.2	74.4	27.7	72.3	61.2	22.1	77.9	66.0
7	14.2	85.8	77.2	59.4	40.6	26.8
8	57.5	42.5	30.4	30.2	69.8	56.0	28.5	71.5	61.6
9	78.3	21.7	8.8	27.3	72.7	62.4
10	69.1	30.9	18.8	17.1	82.9	76.0	32.5	67.5	58.4
11	36.0	64.0	53.2	61.8	38.2	32.4
12	83.2	16.8	7.2						
13	74.3	25.7	13.2						
14						
15	80.7	19.3	10.8						

A. I. R. = Anhydrous insoluble residue.

Sol. = Solubility in water (approximately 20° C.).

A. A. E. = Anhydrous aqueous extractive at 20° C.

COMMENTS.

The solubilities in cold water and the cold water extractive were obtained by the following process:

One gram of the powdered drug (not coarser than No. 40) is macerated for 2 hours in about 50 cc. of water at approximately 20° C. and frequently shaken or stirred. Obtain the complete undissolved residue upon a tared filter, washing with sufficient water to make 100 cc. of filtrate. Dry the residue on the filter to constant weight. The difference obtained by deducting the weight of the anhydrous insoluble residue from the weight of powdered drug taken, expressed in percentage, gives the solubility of the drug in water at 20° C.

Evaporate on a water-bath in a suitable tared dish, an aliquot part of the clear filtrate to a residue and dry the same at 102° C. to constant weight. The weight of the dried residue expressed in percentage of the weight of powdered drug taken gives the anhydrous cold water extractive.

Under Kino, the statements of the U. S. P. and B. P. and N. D. are correct but not very specific. A fresh kino will usually meet the requirements of Greenish, 80-90% soluble.

The requirement of the U. S. P. for gambir, namely, not less than 65% soluble, might well be raised to 75%, the figure named by the N. D. The 85% figure of Kraemer seems to be high.

The three most recent samples of catechu were above 90% soluble, and the fourth sample above 80% soluble. The other samples ranged from 38% to 78%.

The principal question in connection with the cold water solubility of these three drugs seems to be whether cold water will serve as a critical criterion of quality as well as hot water. There is no question but that cold water is easier

to use, not only because of the employment of less apparatus and less manipulation but because the results of repeated operations in various hands are much more uniform than when boiling water is used. Especially does this apply to gambir, where with hot water the filtration is frequently very slow and difficult, sometimes requiring 24 hours in the hot apparatus to complete the filtration of 100 cc. Furthermore, while the solubility of gambir in cold water is about 10 or 12 points less than in hot water, yet the results from cold water are just as uniform as those from hot water; 60 per cent. of cold water extract would insure a good quality of gambir.

SOLUBILITY IN ALCOHOL.

Kino.			Gambir.			Catechu.		
U. S. P.—not less than 45% extractive.			U. S. P.—not less than 60%.			B. P.—not less than 60%.		
B. P.—almost entirely.			B. P.—not less than 80%.			Kr.—70%.		
Gr.—almost entirely.			Gr.—not less than 80%.			N. D.—60%.		
N. D.—entirely.			Kr.—not less than 70%.			G. P.—insol. residue not more than 30%.		
E. N. G.			E. N. G.			E. N. G.		
A. I. R.	Sol.	A. A. E.	A. I. R.	Sol.	A. A. E.	A. I. R.	Sol.	A. A. E.
1	0.3	99.7	30.2	69.8	61.5	17.1	82.9	72.4
2	40.1	59.9	27.6	72.4	62.5	36.1	63.9	58.4
3	56.2	43.8	16.1	83.9	75.0	59.0	41.0	36.0
4	19.0	81.0	18.8	81.2	70.5	28.6	71.4	63.0
5	24.7	75.3	30.9	69.1	60.0	29.1	70.9	62.8
6	59.3	40.7	26.2	73.8	65.0	39.0	61.0	48.5
7	36.2	63.8	67.0	33.0	20.5	59.5	40.5	29.0
8	25.9	74.1	22.6	77.4	70.0	81.9	18.1	8.0
9	70.5	29.5	32.6	67.4	58.5	70.1	29.9	21.5
10	23.5	76.5	25.3	74.7	68.0	78.3	21.7	11.5
11	56.5	43.5	42.9	57.1	46.0	74.4	25.6	14.5
12	79.4	20.6						
13	83.9	16.1						
14	58.0	42.0						
15	61.9	38.1						

COMMENTS.

The solubility in alcohol and the alcoholic extract were determined by the same procedure as the solubility in cold water and the aqueous extract, except that alcohol (95%) was used for the extraction.

Kino, almost universally claimed to be almost entirely soluble in alcohol, always left a marked insoluble residue with us. Only one of the samples examined, sent to us as a recent importation, was over 90% soluble. Other samples, but two or three years old, were only 40%, 60% or 75% soluble, and samples up to 25 years old were down to but 16% soluble. The U. S. P. standard of not less than 45% of alcoholic extractive might be increased to some extent.

One specimen obtained from a New York importing firm last year and claimed to be 90% soluble in alcohol was found to contain 59.2% of anhydrous insoluble residue and therefore possessed a solubility in alcohol of about 40%. In comparison with other samples of known age, this sample was probably 5 years old when we examined it. The firm's chemist undoubtedly examined it soon after importation. Its solubility in alcohol might have decreased this much in 5 years.

To test further the alcoholic solubility of this sample, we macerated in a water-bath 1 Gm. of No. 40 powder in 40 cc. of alcohol, in a 125-cc. flask with a reflux condenser for 2 hours, filtered and dried as indicated above. The anhydrous insoluble residue was 58.9%, a difference by the use of hot alcohol for 2 hours of 0.3%. Furthermore, we prepared flasks with 1 Gm. of the powder in each and treated them as indicated above with cold alcohol, except that the maceration in alcohol was only 20 minutes for the first flask and was lengthened 20 minutes for each succeeding flask to 360 minutes for the last flask. The anhydrous insoluble residue from the first flask was 73.5%, from the last flask 58.0%. The graduation of the residues was not perfect, yet fairly good; it is evident that after 2 hours, further maceration is of no value. The solubility of kino in alcohol is a criterion of its age and its value.

Gambir in alcohol seems to run about half way between the 60% limit of the U. S. P. and the 80% limit of the B. P. Of the 11 samples examined 2 were above 80%, 4 were between 70 and 80%, 3 were between 60 and 70%, and 2 were below 60%.

Catechu, like kino, is less soluble in alcohol upon aging. Of the eleven lots examined only three gave less than 30% insoluble residue, the G. P. limit, and but five exceeded 60% solubility, the B. P. limit.

SOLUBILITY IN DILUTED ALCOHOL.

	Kino.		Gambir.			Catechu.			
	A. I. R.	Sol.	A. A. E.	A. I. R.	Sol.	A. A. E.	A. I. R.	Sol.	A. A. E.
1	5.8	94.2	80.8	15.3	84.7	75.0	2.0	98.0	86.0
2	3.2	96.8	85.2	15.2	84.8	76.5	7.2	92.8	86.0
3	8.7	91.3	80.0	7.8	92.2	83.6	6.4	93.6	84.0
4	11.5	88.5	76.0	7.1	92.9	83.5	3.5	96.5	88.0
5	18.8	81.2	69.2	14.3	85.7	76.0	21.2	78.8	69.2
6	12.0	88.0	79.2	12.5	87.5	75.2	18.5	81.5	68.8
7	2.3	97.7	88.4	72.6	27.4	21.5
8	25.3	74.7	63.2	9.4	90.6	79.5	22.1	77.9	66.4
9	61.1	38.9	26.8	12.2	87.8	71.5	22.4	77.6	68.0
10	27.0	73.0	62.8	3.1	96.9	82.0	22.2	77.8	68.0
11	61.8	38.2	30.4	17.3	82.7	71.2	10.3	89.7	78.0
12						
13	44.2	55.8	45.2						
14						
15	53.3	46.7	34.4						

COMMENTS.

The solubility in diluted alcohol and the anhydrous diluted alcohol extractive were obtained by the same process employed for determining the solubility in alcohol and the alcoholic extractive, except that diluted alcohol, U. S. P., was used to extract the drugs.

The percentage of solubility in diluted alcohol of each sample of each drug is usually somewhat less than in boiling water, and considerably more than that in alcohol.

The solubility of the seven more recent samples of kino ranged from 97.7 to 81.2%, the eight older samples being much less soluble. An extractive standard of 75% would include all of the kino of value.

The gambir samples were soluble, with one exception, to the extent of 82.7 to 92.9%. An extractive standard of 70% would exclude but one of the 11 samples examined and 75% would exclude only the 3 poorest samples.

Black catechu likewise is quite soluble in diluted alcohol, the range of the 11 samples being from 77.6 to 98.0%. An extractive standard of 75% would exclude 5 of the 10 samples examined. A standard of 65% would include all of the samples examined.

The method of preparing Tincture Gambir Compound as presented in the U. S. P. which calls for maceration in diluted alcohol for three days and subsequent filtration, apparently cannot be improved, for the extractive obtained, on the average, with diluted alcohol equals that obtained with hot water and exceeds that obtained with cold water or strong alcohol.

Also the method for preparing Tincture of Kino as presented in the U. S. P. which calls for extraction with hot water kept on the water-bath for an hour, filtration and the subsequent addition of an equal volume of alcohol is very good, for not only is the troublesome enzyme which causes gelatinization destroyed but the kino is dissolved to the greatest extent by hot water.

CONCLUSION.

1. The ash of kino is found frequently to run higher than the 2.5% allowed by the British Pharmacopœia or even the 3% of the U. S. P. Likewise the ash of black catechu in all instances exceeded the 5% limit of the British Pharmacopœia and in only one case was lower than the 6% permitted by the German Pharmacopœia. On the other hand, the ash of gambir was invariably lower than the 9% limit of the U. S. P. and usually lower than the 5% of the British Pharmacopœia.

2. If the percentage of the hydro-alcohol-soluble astringent constituents of kino, gambir and black catechu is a criterion of the therapeutic value of these astringent drugs, then kino markedly deteriorates upon aging, catechu does so to some extent, but gambir shows but slight change in this respect.

3. A good quality of kino or black catechu is at least 90% soluble in boiling water and gambir at least 85% soluble in boiling water. Samples of kino more than a few years old are less soluble, some old lots of kino being only 30% to 40% soluble in boiling water.

4. As catechin to the extent of 20–40% is claimed to be present in catechu and gambir and to be insoluble in cold water, a marked falling off in the cold water solubility of these drugs might be expected. This decrease in solubility as compared with the solubility in boiling water was, on the average, 16%. Kino, which is said to contain but little kinoin which is likewise insoluble in cold water, however, also showed a decrease of 16% as the average of the seven most recent samples.

As the cold water solubility of gambir is quite as uniform as that in boiling water and because of the great difficulty in filtering a hot aqueous gambir mixture, it is recommended that the solubility of gambir in cold water be preferred to that in hot water as a criterion. A requirement of 75% would exclude but the 4 poorest of the 11 samples examined.

5. While kino is generally credited with being almost entirely soluble in alcohol, only one specimen of the 15 examined was 90% or more soluble in alcohol. This kino was of recent importation. Aging even of one or two years decidedly

reduces the solubility in alcohol and long aging renders the kino almost insoluble. As a criterion of quality, if the requirement is put high, 90%, where it should be, kino must be used immediately upon importation or some means be found for its preservation against deterioration. If put low, 60%, its value as a criterion is doubtful.

Gambir in alcohol easily met the 60% solubility requirement of the U. S. P., but only two samples out of eleven met the 80% requirement of the British Pharmacopœia. A standard of 65% would be satisfactory.

Of catechu, but three samples out of eleven met the German Pharmacopœia requirement of 70% solubility in alcohol and but 5 samples met the 60% requirement of the British Pharmacopœia.

6. The percentage of solubility in diluted alcohol of each sample of each drug is usually somewhat less than that in boiling water and considerably more than that in alcohol.

7. The anhydrous extract as a constant has an advantage over the solubility determination in that it is not influenced by moisture in the drug.

An anhydrous hot water extractive standard of 80 per cent. for kino, 75 per cent. for catechu and 75 per cent. for gambir would insure satisfactory drug.

An anhydrous cold water extractive standard of 60 per cent. would be satisfactory for kino or catechu and especially so for gambir.

An anhydrous alcoholic extractive standard of 60 per cent. for gambir might be a valuable criterion. The present U. S. P. standard of not less than 45 per cent. for kino seems low, but cannot be appreciably raised without excluding all but the most recent importations of kino. The same standard might be used for catechu.

A standard of 75 per cent. of anhydrous diluted alcohol extractive would insure a good quality of kino, gambir or catechu.

8. The anhydrous insoluble residue as a criterion of quality of these drugs has the following advantages over either the solubility or the anhydrous extract:

- 1.—Most easily and accurately obtained.
- 2.—Not affected by the percentage of moisture in the drug.
- 3.—Most critical.

Suitable standards would be as follows:

	Kino.	Gambir.	Catechu.
From boiling water	10%	15%	10%
From cold water	30%	30%	30%
From alcohol	35%	35%	35%
From diluted alcohol	20%	20%	20%

9. The U. S. P. methods for the preparation of Tincture Kino and Tincture Gambir Compound embody the best means for extracting the respective drugs and apparently cannot be improved upon.

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