

THESIS

on

THE STRENGTH OF COMMERCIAL TINCTURE OF OPIUM AS COMPARED WITH THAT
OF THE UNITED STATES PHARMACOPOEIA.

Submitted by the Faculty of

the

O R E G O N A G R I C U L T U R A L C O L L E G E .

for the degree of

Bachelor of Science.

by

Redacted for Privacy

Redacted for Privacy

Approved

Redacted for Privacy

Dept.

Redacted for Privacy

THE STRENGTH OF COMMERCIAL TINCTURE OF OPIUM AS
AS COMPARED WITH THAT OF THE UNITED STATES
PHARMACOPOEIA.

Laudanum is the commercial name of "Tincture of Opium", or "Tinctura Opii", as recognized by the United States Pharmacopoeia. It contains 10% granulated opium, one of the most powerful and common hypnotics known, or from 1.2 to 1.25 % of morphine sulphate, the principal alkaloid found in opium and to which its medicinal activity is largely due.

Opium is the dried milky juice exuding from the excised unripe seed capsules of the poppy, *Papaverae somniferum*, Natural order Papaveraceae, cultivated in Asia and Egypt. It is very complex, containing about twenty-one alkaloids, all of which are more or less potent. // The granulated Opium from which the tincture is made contains from 12 to 12.5% morphine, .2 to .7 % Codeine, .15 to 1% Thebain, .02 to .7 % Narcein, 1% Papaverin, and 1.3 to 10% Nariotin as required by the U.S.P.

Opium and its preparations form a class of the most potent drugs known to medicine, being used as a hypnotic, anodyne, antispasmodic and diaphoretic. An overdose causes acute poisoning and after death. Death has been known to result from the dose of $\frac{1}{4}$ gr. morphine (rare) in an adult. Children are very susceptible to its action, and care must be used in its administration to

prevent the formation of the dreaded opium or morphine habits.

Tincture of Opium is used as a hypnotic, to induce sleep; as an anodyne, to allay pain, or as a sedative, to quiet the nerves. It is used both internally and externally being used to stop pain in ear-ache etc. Its dose is from twelve to twenty-four drops. An overdose produces poisoning and death resulting with stupor and coma. Its sale by pharmacists is governed by law and it is required to be registered as a poison when sold. It is obvious, therefore, that it must be known strength, upon which the physician can rely when he prescribes it. If it be too strong, there is danger of an over-dose.

The Pharmacopoea of the U.S. requires that it shall contain not less than 1.2% nor more than 1.25 % crystallizable morphine; according to the U.S.P. assay.

The object of this thesis is to ascertain the strength of "Tincture of Opium" that is used by the pharmacists of Oregon, according to the assay prescribed by the U.S.P. Accordingly a number of samples were collected from representative sections throughout the state of Oregon. The U.S.P. assay is as follows:

The materials used are,

Tincture of Opium 10000s.

Ammonia Water 35 "

Alcohol

Ether

Water

Lime Water

aa

q. s.

Transfer one-hundred ccs of Tincture of Opium to an evaporating dish and evaporate it on a water bath to about twenty ccs, add forty ccs of water, and set the liquid aside for an hour occasionally stirring to disintegrate the resinous flakes adhering to the sides of the dish.

Then filter the liquid and wash the filter and residue with water until all soluble matter is extracted which is indicated by an almost colorless filtrate, and collect the washings separately. First evaporate the washings in a tared dish, to a small volume, then add the first filtrate and evaporate the whole to a weight of fourteen grams. Rotate the concentrated solution about in the dish until the rings of extract are redissolved, pour the liquid into a tared Erlenmeyer flask, having a capacity of about one-hundred ccs, and rinse the dish with a few drops of water at a time until the entire solution after the rinsings have been added to the flask weigh twenty grams. Then add ten grams or twelve and two tenths ccs of alcohol, shake the flask well, add twenty five ccs of ether, and repeat the shaking. Now add 3.5 ccs of Ammonia Water (10%), stopper the flask with a sound cork, shake it thoroughly during ten minutes and then set it aside in a moderately cool place for at least six hours or over night.

Remove the stopper carefully and should any crystals adhere to it brush them into the flask. Place in a small funnel two rapidly acting filters of seven centimeters in diameter plainly folded, one within the other (the triple fold of the inner filter being laid against the outer), wet them well with ether and decant the ethereal solution as completely as possible upon the inner filter. Add 10 ccs of ether to the contents of the flask, rotate it, and again decant the ethereal layer upon the inner filter. Repeat this operation with another 10 ccs of ether, after which pour the liquid in the flask upon the filter in such a way as to transfer the greater portion of the crystals to the filter and when the liquid has passed through, transfer the remaining crystals to the filter by washing the flask with several portions of water, using not more than 15 ccs in all. Use a feather or a rubber-tipped glass-rod to remove the crystals that adhere to the flask. Allow the double filter to drain, then apply the water to the crystals drop by drop, until they are practically free from mother liquor, and afterwards wash them drop by drop, from a pipette, with alcohol previously saturated with powdered Morphine. When this has passed through displace the remaining Alcohol by ether, using about 10 ccs or more is necessary. Allow the filter to dry in a moderately dry place at a temperature not exceeding 60° C. (140° F.) until its weight remains constant,

then carefully transfer the crystals to a tared watch-glass and weigh them.

Place the crystals (which are not quite pure) in Erlanmayer flask, add lime water (10ccs for every 1/10 gram of Morphine) and shake the flask at intervals during $\frac{1}{2}$ and hour. Pass the liquid through two counterpoised, rapidly acting filters, rinse the flask with lime water and pass the washings through the filter until the filtrate, after acidulating no longer yields a precipitate with Mercuric Potassium Iodide (absence of Morphine). Press the filters until nearly dry between bibulous paper and dry them to a constant weight, then weigh the contents, using the outer filter as a counterpoise. Deduct the weight of the insoluble matter on the filter from the weight of the impure Morphine previously found. The result will represent the grams of crystallized Morphine yielded by 100ccs of Tincture of Opium.

EXPLANATION OF THE ASSAY.

1. This assay is based upon the process of alkaloidal assay by immiscible solvents. Morphine exists in Opium in the form of Morphine Sulphate, the Morphine is changed to alkaloidal Morphine, insoluble or nearly so in water, ether, or alcohol, which is precipitated. As the original tincture is an Alcoholic solution, it is first evaporated to drive off the Alcohol then treated with

water to extract the Morphine Salt.

SOURCES OF ERROR

1. Lime Water under certain conditions has a tendency to dissolve certain impurities as well as the Morphine Sulphate, existing in the Morphine.
2. Incomplete conversion of the salt into the alkaloidal form by the Ammonia Water.
3. Incomplete extraction of the Tincture by water.

All filtrates in the assay should be tested for Morphine Sulphate by allowing it to drop into a white dish containing about 3 ccs concentrated Sulphuric Acid and 4 drops Formaldehyde. If Morphine be present it is shown by a beautiful violet color.

In all, seventeen samples were collected and assayed with the results as stated below. The only variation from the U.S.P. assay taken was in cases where sufficiently large samples were not obtainable, sixty and seventy-five ccs of the samples were used instead of one-hundred ccs. This however did not cause any great error as the following results will show.

Source	Amount used	Amount of impure Morphine found	Amount of Impurities	Weight of pure Morphine	Wgt. in 100 ccs	Wgt. required by U.S.P.
1. HoodRv	75 ccs	.4874 gm	.007 gm	.4404 g	.5873m	1.2-1.3
2. "	"	.6991	.0043	.6948	.9265	"
3. "	"	.6440	.0013	.6428	.8571	"
4. Silverton	60 ccs	.5448	.0094	.5354	.8590	"
5. "	"	.6629	.0071	.6558	1.093	"
6. Baker C	"	.6791	.0084	.6707	1.12	"
7. "	"	.4045	.002	.4034	.6723	"
8. Richland	"	.69859	.003	.69558	1.159	"
9. Athena	"	.2112	.0055	.2057	.3428	"
10. Baker C	"	.44	.0025	.4375	.7292	"
11. Salem	No test	even for	Morphine			
12. Salem	60 ccs	.4429	.0021	.4464	.735	"
13. Albany	100	1.315	.034	1.281	1.281	"
14. "	90	.7306	.0010	.7296	.8107	"
15. "	60	.6409	.001	.6699	1.12	"
16. McMinn.	50	.4567	.0079	.4488	.8976	"
17. Corvallis	100	1.235	.011	1.224	1.224	"

The above results show the majority of samples to be far below the standard. Out of the total 17 samples, but one sample, No 13, yielded as much as ϕ 1.2 gm. of Morphine Sulphate. The rest range from 50 to 85% of the strength required by the U.S.P. This illustrates forceably the handicap which physicians are placed in in prescribing their preparations.

In order to prove that the U.S.P. assay was not at fault, sample 17, made strictly according to the formula, was assayed and proved to be standard. The U.S.P. process for the manufacture of Tincture of Opium is as follows:

Granulated opium 100 gm.
 Alcohol
 Water
 Dilute Alcohol $\bar{a}\bar{a}$ Q.S. 1000 gm.

Heat 400 ccs of water to boiling and pour it in upon the granulated Opium contained in a tared vessel and stir occasionally during twelve hours; then restore the original weight by the addition of cold water, add 400 ccs of alcohol, pour the mixture into a bottle and continue the maceration for 48 hours, occasionally shaking. Transfer the mixture to a percolator, return the first portion of the percolate until it runs through clear, and when the liquid ceases to drop, continue the percolation slowly, pouring on sufficiently diluted Alcohol until 1000 ccs are obtained.

Because of such a large discrepancy in the commercial tinctures can be assigned to one or all of two reasons; namely,

1. The U.S.P. method not followed properly.

Imperfect maceration and percolation may not extract all of the Morphine in the Opium.

2. The use of a poor grade or an adulterated sample of Opium, which has been adulterated by the druggist.