UNITED NATIONS

ECONOMIC
AND
SOCIAL COUNCIL

GENERAL

E/CN.7/207
19 October 1950

ORIGINAL: ENGLISH

Commission on Narcotic Drugs
Fifth session
Item 12 of the provisional agenda

METHODS OF DETERMINING THE ORIGIN OF OPIUM BY CHEMICAL AND PHYSICAL MEANS

Further Data on "Porphyroxine-Meconidine"

Note by the Secretary-General

The Government of Canada has decided to participate in the international programme of research to develop methods for determining the origin of opium by chemical and physical means, which the Secretary-General has undertaken pursuant to Resolution 246 F (IX), adopted by the Economic and Social Council on 6 July 1949.

A programme of research was accordingly instituted by members of the Organic Chemistry and Narcotic Section of the Food and Drug Divisions, Department of National Health and Welfare. Work was begun 11 December 1949, and the Secretary-General now has the honour to transmit herewith the first technical paper covering work by the Canadian chemists, entitled "Further Data on 'Porphyroxine-Meconidine'". This work was begun and largely carried out before the publication of the first technical paper by the United Nations chemists, "The Comparative Determination of 'Porphyroxine-Meconidine'", E/CN.7/195, which, in general, it confirms.

/FURTHER

FURTHER DATA ON "PORPHYROXINE-MECONIDINE"

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I. OBJECT

1. The object of this paper is to show confirmation of the United Nations results in regard to variations of "porphyroxine-meconidine" with origin, and to report on some of our original researches.

II. SAMPLES USED

2. These were samples from some of the same opiums used by the United Nations chemists. They were supplied by the United States Government through the kind co-operation of the Narcotic Control Division, Department of National Health and Welfare, Ottawa, Canada, and the Narcotics Bureau of the United States Treasury Department, Washington, D.C. The co-operation of officials in these agencies and the help of Dr. L. I. Pugsley and Dr. C. A. Morrell of the Food and Drug Divisions Department of National Health and Welfare, Canada, is gratefully acknowledged.

3. The samples analysed were all weighed in the air-dried condition.

III. METHOD FOR TABULATED ANALYSES

4. The method used was based on the one developed originally by Fulton and given in E/CN.7/117/Add.2, page 16. Some modifications of our own were introduced. The method as finally used was the same as that given in E/CN.7/195, with the following partial exceptions:

The mixture of water, lime, and opium, was stirred in the mortar for one hour. The ether used was first freed from peroxides by shaking with acidulated ferrous sulfate solution. The filtered aqueous solution was extracted continuously with ether about four and one-half hours, until a negative test for "porphyroxine-meconidine" was obtained with the return ether. The ether was then recovered by redistillation, the residue remaining in the flask. The color was developed by treating the residue with 5 cc 1 vol.% Hcl and heating at 80°C for about twenty minutes. The solution was then poured into a 10 cc. volumetric flask and rinsed in with additional small portions of dilute Hcl, warmed in the flask, until the total volume was 10 cc. The colour was read by means of the Lovibond tintometer, usually in the 1/16 inch cell. The results were, therefore, multiplied by two to correspond to the United Nations results (E/CN.7/195). When necessary, the solution was diluted further, always with the 1% Hcl, and the reading multiplied accordingly.

/IV. TABULATION

IV. TABULATION OF RESULTS

5. The following table gives the color values found, in red Lovibond units.

India

Baroda State	7.8
Old seizure of Gwalior biscuit opium	7.8
Mewar State	9.2
U.S. seizure from "Silverwalnut", San Francisco	11.4
Tonk State	20.0
Indore State	20.4
Gwalior State	20.6
Seizure of standardized opium	22.0
Ratlam State	22.8
Export 43385, Merck 1944	24.2
U.S. seizure from "Silverwalnut" at Seattle	26.2
Export 63913, Mallinckrodt 1944	26.4
Dewas Junior State	26.4
Piploda State	29.2
Jaora State	30.2
Partabgarh State	30.6
Export 44121, Mallinckrodt 1944	32.0
Sailana State	40.0
United Provinces	40.0
Sita Mau State	43.4
A State of East Punjab	44.0
A Punjab Hill State	52.0
Kotah State	54.4

Afghanistan

Export 63910, Mallinckrodt 1943	8.0
Export 63909, Mallinckrodt 1943	12.2

Yugoslavia

Export 63915, Mallinckrodt 1938	4.0
Export 44125, Mallinckrodt 1941	7.2
Export 63914, Mallinckrodt 1943	7.4

/Far Eastern

Far Eastern Countries

Mongolia	8.8
China (Manchuria)	9.6
Singapore stocks ("Malayan")	13.2
Korea	15.2
Japan	65.0

Turkey

Sandikli	4.2
Isparta	6.4
Malatya	8.4
Corum	8.6
Export 44123, Mallinckrodt 1944	8.6
Sinav	9.0
Seizure of standardized	9.0
Export 63911, Mallinckrodt 1946	9.8
Usak	10.2
Export 44124, Mallinckrodt 1944	10.4
Provincial name lost, probably Afyon	11.4

Iran

Kermanshah	1.6
Khorassan	2.2
Sticks, purple-red labels	2.6
Isfahan	3.0
Fars	4.5
Export 63409, Merck 1947	4.6
Lorestan	6.4
Export 63916, Mallinckrodt 1944	6.4
Sticks, blue-green labels	7.6
Kerman	7.8
Malayer	7.8

/V. DISCUSSION

V. DISCUSSION OF TABULATED RESULTS, AND GRAPHS

6. Our results average somewhat lower than the United Nations results for the same samples, but are of the same general magnitude, and show exactly the same classification:

India -- generally high to very high
(nineteen samples out of twenty-three with colour value 20 or more, up to 54.4)

Iran -- medium low to very low
(values 7.8 down to 1.6; eight samples out of eleven less than 6.5)

Other countries -- generally intermediate

With the exception of the Japanese sample, which, as in the United Nations results, was highest of all (65.0-67.2), no non-Indian sample in our possession yielded a value greater than 15.2. For values below 15.3, with only three exceptions out of twenty-three samples, from countries other than Iran the results were above 6.5; therefore only in small part overlapping the Iranian values.

7. The general comparison of our results with those of the United Nations chemists is shown in the accompanying graphs. (See Annex I.)

8. The maximum discrepancies in different classes of readings between the United Nations results and ours were the following:

Class by our results:	UN result	Our result	Difference
High values, above 20: United Provinces (India)	53.1	40.0	-13.1
Intermediate values: Malayer (Iran)	15.5	7.8	- 7.7
Low values, less than 6.5: Isfahan (Iran)	8.0	3.0	- 5.0

In both the last two results, our lower values are more normal for Iran than the United Nations results on these particular samples.

9. In considering possible reasons for discrepancies two points should be especially noted:

(i) Our results in general were lower; if any correction is applied for this, the magnitude of any large negative discrepancy is correspondingly reduced;

/(ii) The

(ii) The original samples were not ground up and thoroughly mixed; it is therefore quite probable that some differences in results are due to actual differences in the portions taken from the original lump of opium.

Other reasons for differences are the following:

(iii) The methods were not quite identical;

(iv) The Lovibond tintometer is rather inaccurate and readings by different observers even on the same solution might possibly differ by as much as 10 per cent of the value.

10. Considering the various reasons for discrepancies, the results correspond quite convincingly. The relation of "porphyroxine-meconidine" values to origin is definite.

VI. NOTES ON THE METHOD

11. The alkalinity of the lime must be satisfactory. Subsequent to some early difficulties we have used freshly slaked lime.

12. It is necessary also that the opium and lime be very well ground up with water and mixed thoroughly. Some of our early experiments in which powdered opium was merely mixed and stirred with lime and water in a beaker by means of a stirring rod, resulted in only about half or less of the "porphyroxine-meconidine" being recovered.

13. In order to secure as complete extraction as possible, we continued the stirring of the opium in lime water solution for one hour before filtration. We have found, however, that if the mixture remains standing more than one hour the results for "porphyroxine-meconidine" are low. Probably there is some oxidation of the phenolic alkaloid in alkaline medium. At any rate it is definite that there is some loss of determinable "porphyroxine-meconidine" from too-long standing at this stage.

14. A decline in the red colour value was found in all cases of prolonged heating of the acid aqueous solution. This confirms a finding of the United Nations chemists.

15. Rakshit remarks concerning his "porphyroxine" that "when its dilute mineral acid solutions are kept exposed to air, they assume a fine pink porphyry colour" -- implying that air (oxygen) is necessary to development of the colour. We therefore tried an experiment to determine if this is the case. Ether containing

/"porphyroxine-

"porphyroxine-meconidine" was evaporated to dryness in a pyrex test-tube, previously drawn down to facilitate sealing off. The residue was covered with 10 cc. dilute HCl, then the solution was at once frozen by immersing the tube in a freezing mixture of dry ice and acetone. The tube was then evacuated of air by means of a vacuum pump. The solution was then melted and the tube pumped out again. This process was repeated several times. Finally the tube was sealed off, warmed slowly to room temperature, then immersed in warm water at 50° C. for several minutes. The red colour developed much as usual, first appearing as a pure pink. In an open tube a solution from the same sample first assumed a light orange tint before becoming red.

VII. EXTRACTION AND pH EXPERIMENTS

16. Opium extraction with water at the natural opium pH and "porphyroxine-meconidine" extraction at various pH values

In a series of experiments the weighed Turkish standardized opium sample was finely ground and then triturated with 40 cc. of water. The pH of this solution was found to be 5.97: after about one hour's standing with occasional stirring the opium-water mixture was filtered. The filtrate was then titrated with the appropriate volume of 0.1M hydrochloric acid or sodium hydroxide base to produce a certain pH value. The pH obtained was measured electrometrically using a model H Beckman meter equipped with a type 015 glass electrode for values 1 to 9 and an E electrode for higher values. This opium solution was then extracted with ether for five and one-half hours, and the pH measured again after removal of the ether. The amount of "porphyroxine-meconidine" obtained was determined by developing the red colour in 10 cc dilute HCl (1 per cent by volume of concentrated HCl) and measuring the colour of the red solution in the 1/16 inch cell of the Lovibond tintometer. The following results were obtained.

cc acid or base added	pH found	pH after ether extraction	Red colour in Lovibond units
7.8 acid	2.30	2.40	0.2
3.14 "	3.12	3.23	0.7
-	4.08	sample lost	-
0.9 "	4.93	4.58	2.4
0.9 "	5.09	4.63	3.2
0.0	5.97	5.10	2.4
1.5 base	7.08	5.59	3.1
4.7 "	8.01	6.01	2.0
10.5 "	9.04	8.90	2.1
15.7 "	10.04	10.50	2.3
19.0 "	11.12	10.63	2.3

/The greatest

The greatest amount of "porphyroxine-meconidine" was extracted in this method between pH 5 to 7. The pHs at the end of the ether extraction were 4.6 to 5.6. There was insufficient buffer action to maintain the pH during the ether extraction. Poor results with pH 3.2 or less suggest that "porphyroxine-meconidine" was changed to an ether insoluble compound, probably the red compound, before it could be extracted. This series shows that "porphyroxine-meconidine" can be extracted to a large extent from an aqueous opium solution without further manipulation at its natural pH value.

17. Extraction of opium and "porphyroxine-meconidine" at various pH values

In this series of experiments acid or alkali was added to the water with which the opium was triturated. The pH of this water extraction of the opium was determined as well as the pH after filtration immediately prior to the extraction of "porphyroxine-meconidine". Then 40 cc of this filtrate representing 1 gramme opium was extracted with ether for five and one-half hours, and the pH again determined after the extraction. The "porphyroxine-meconidine" obtained was determined by developing the colour in 10 cc dilute HCl and measuring it in the 1/16 inch cell of the Lovibond tintometer. The following results were obtained:

cc acid or base used	pH of solution used	pH of opium solution	pH after extraction	Red colour in Lovibond units
9.7 HCl	1.62	2.80	2.62	0.8
3.7 "	1.96	4.25	3.78	3.2
1.9 "	2.24	4.85	4.48	3.4
0.8 "	2.60	5.86	4.71	3.3
0.1 NaOH	9.78	5.78	5.81	2.5
1.5 "	11.36	6.42	5.42	2.6
2.5 "	11.60	7.42	5.80	2.5
10.5 "	11.92	8.42	7.46	3.2
15.7 "	12.06	9.05	8.90	3.8
19.1 "	12.10	9.47	9.58	4.3

The first result is low because of the conversion of "porphyroxine-meconidine" to the red compound before it could be extracted by the ether. The aqueous solution at pH 5.8 to 7.4 contained considerably less "porphyroxine-meconidine" than at either higher or lower pH values. Highest values were obtained from the acid solution of pH 4.85 (4.48 after the ether extraction) and pH 9.47 (9.58 after the ether extraction). This was the highest pH tried in this series of experiments.

/VIII.

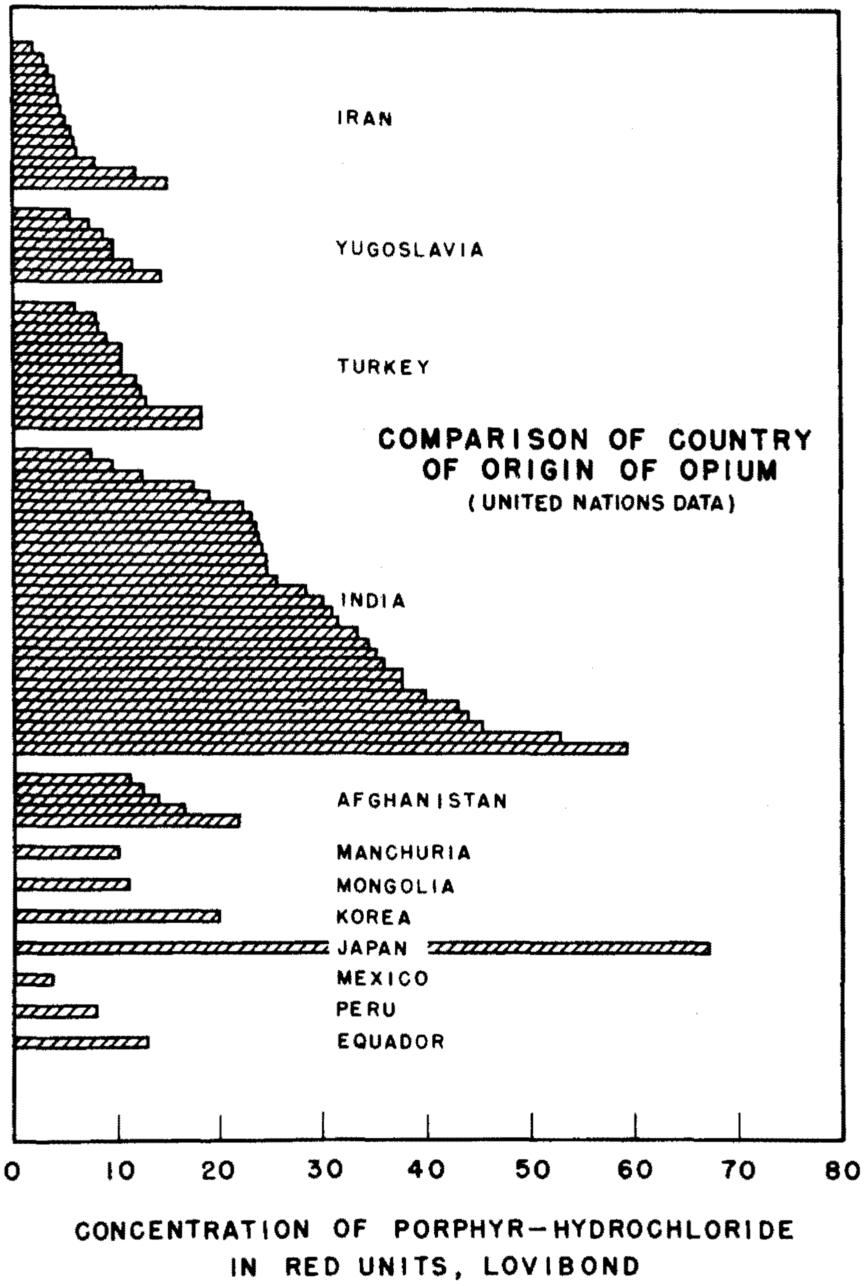
VIII. SPECTROPHOTOMETRIC CURVES OF "PORPHYR"

18. The absorption spectrum of the "porphyr", the red compound formed, has been measured, using the Beckman DU Model spectrophotometer. The important maxima occur at 283-287 mμ (U.V.) and 505 to 520 mμ (green); but it seems possible that the former is really due to cryptopine. The latter has been chiefly used in this work. This peak is sharp, extent of about 2 mμ, and thus should provide excellent sensitivity for a quantitative method. The curves obtained are similar for all the opiums tested so far, that is all the peaks occur at the same places with all the opiums tested.

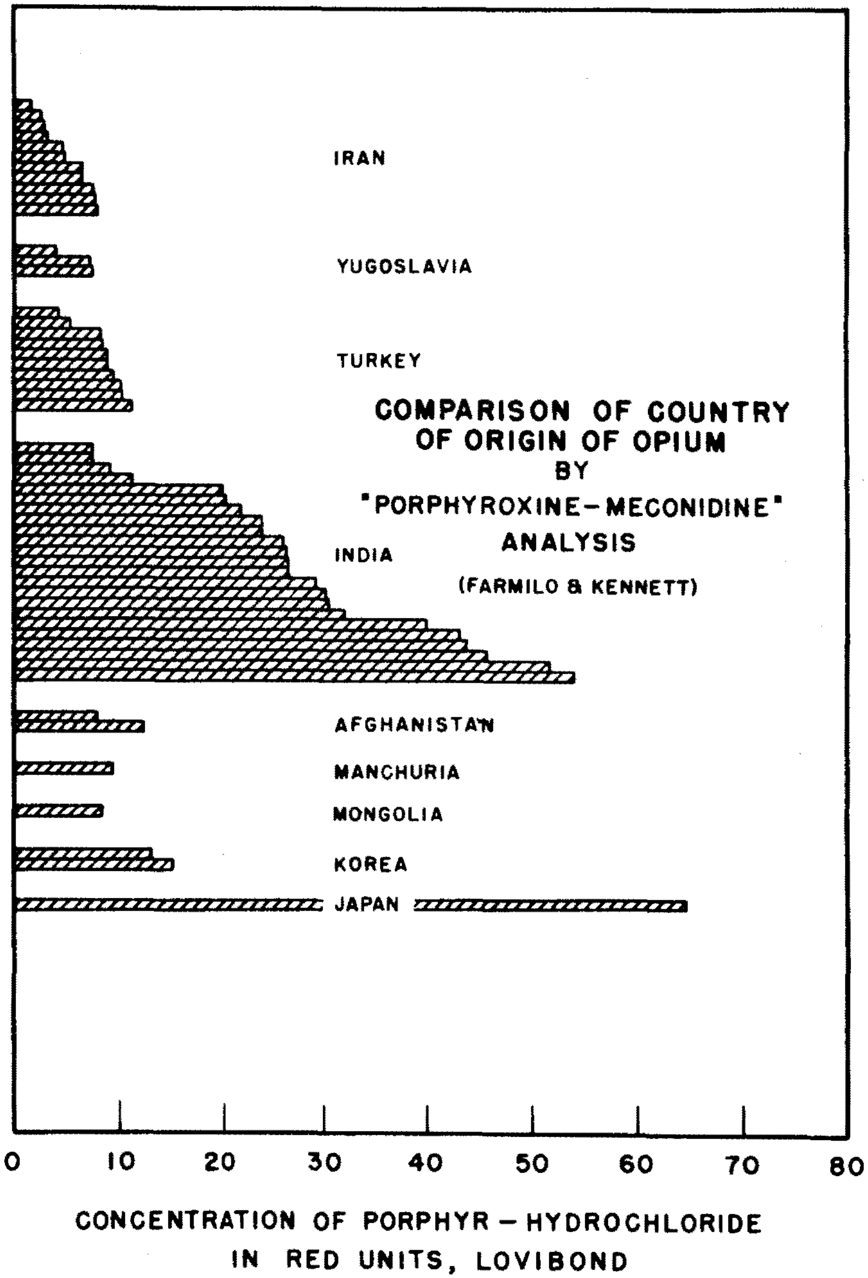
IX. CONCLUSIONS

19. The method has great value for indicating the origin of opium. The opium from India usually yields a high to very high value, that from Iran usually low to very low. Intermediate values are characteristic of the opiums from Turkey and Yugoslavia, but occur also in most other countries, even including Iran and India. The greatest value is in demonstrating Indian origin. In our tests no non-Indian sample, except the Japanese one, was found to yield a higher value than 15.2, whereas nineteen of twenty-three Indian samples yielded values of 20 or more.

20. Our experiments indicate that more work could profitably be done to arrive at the best method of extracting the "porphyroxine-meconidine" from the opium and then from aqueous solution, and converting it to the red compound. Results should be accurately quantitative - at least in a comparative sense - and easily reproducible. We intend to do more work on this problem.


COMPARISON OF COUNTRY OF ORIGIN OF OPIUM

(UNITED NATIONS DATA)


COMPARISON OF COUNTRY OF ORIGIN OF OPIUM BY "PORPHYROXINE-MECONIDINE" ANALYSIS

(FARMILO & KENNETT)