by the oxidation of MPZ oxalate with 30% hydrogen peroxide. The MPZ sulfoxide oxalate melted at 208–210°C under decomposition and the free base melted at 93–94°C. Infrared analysis showed strong absorption at 9·82 μ which indicates the presence of a sulfoxide group. The U.V. absorption curve of the MPZ sulfoxide base in absolute ethanol showed maxima at 242, 253·5, 277, 296·5, and 335 mμ, which seems to be characteristic for aminoalkylphenothiazine sulfoxides. The MPZ sulfoxide in aqueous solution (acetate buffer pH 5·6 acidified with sulfuric acid) showed the same maxima as given above for the metabolite (Fig.).

Urine and concentrated ethereal extracts were also analysed by paper chromatography (Whatman 1, descending in (A) butanol-acetic acid-water, 40:10:50 and (B) butanol-citric acid-water on paper treated with citrate buffer pH 3·7, according to CURRY and POWELL[6]). Spots were identified (1) by U.V. illumination[7] of the paper with a fluorescein screen as background and (2) by immersion of the paper strips rapidly in 50% sulfuric acid[3] containing 0·25% ferric chloride, which gives coloured spots with a number of phenothiazine derivatives. The sensitivity of both methods is about 1 μg MPZ per cm². MPZ showed R_f 0·83 in solvent (A) and 0·73 in solvent (B) (mean values). With urine and ethereal extracts from urine of patients treated with MPZ, a main spot with R_f 0·69 in solvent (A) and 0·45 in solvent (B) was obtained, which showed U.V. absorption and the sulfuric acid reaction. MPZ sulfoxide standard showed identical properties. After elution of the spot in solvent (A) in 0·1 *N* sulfuric acid solution, a U.V. absorption curve identical with that of the synthetic MPZ sulfoxide, was obtained.

In addition, a spot corresponding to MPZ was obtained in the two solvents although the intensity varied in the different cases. In general it was less intense than the sulfoxide spot.

Quantitative analyses by extraction[3] and U.V. spectrophotometry have shown that up to one third of the MPZ dose given is eliminated in the urine, mainly as the sulfoxide.

Additional spots, showing U.V. absorption and the sulfuric acid reaction, were obtained with urine in some cases. R_f values were below 0·3.

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Zusammenfassung

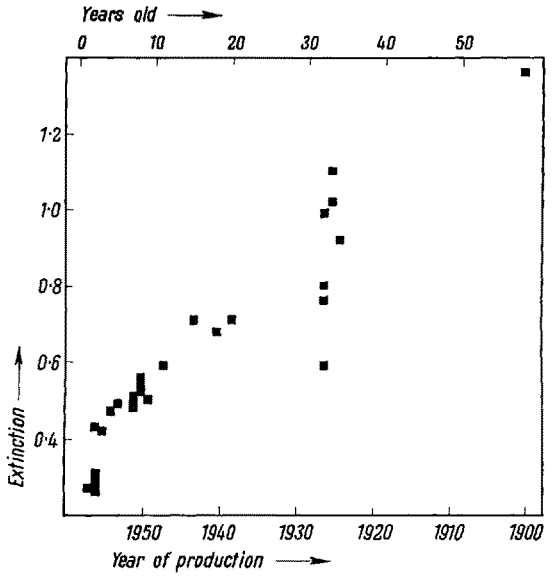
Die Ausscheidung eines neuen neuroleptisch wirksamen Phenothiazinderivates – Mopazin – im Harn wurde spektrophotometrisch und papierchromatographisch untersucht. Als wichtigstes Abbauprodukt wurde Methoxypromazin-sulfoxyd gefunden. Daneben waren unverändertes Methoxypromazin und 1–3 nicht identifizierte Abbauprodukte nachzuweisen. Bei den letzteren handelt es sich möglicherweise um Konjugate.

[6] A. S. CURRY and H. POWELL, Nature *173*, 1143 (1954).
[7] L.-G. ALLGÉN, Scand. J. clin. Lab. Invest. *9*, 71 (1957).

On the Possibilities of Estimating the Approximate Age of Macedonian Opium by Means of a Simple Colour Reading

In the course of the work on the direct spectrophotometric determination of opium origin performed in this laboratory[1], it has been observed that the yellow colour of the buffered water extracts of various types of opium was relatively intense in old samples, whereas recent samples generally exhibited only slightly coloured extracts. For this reason, an attempt was made to examine in detail the relationship between the yellow colour of the extracts and the year of production of samples belonging to a certain opium type. The determination of the approximate year of production of seized opium may be of great importance in a successful campaign against the illicit traffic of narcotics.

The present report concerns the results obtained by examining 41 samples of Macedonian opium (39 Yugoslavian and 2 Bulgarian) which were from 1 to 58 years old.



Relationship of the extinction values at 440 mμ and the age of the samples examined

(Samples having the same values on both the ordinates, as well as those showing nearly the same extinction values, overlap each other and therefore cannot be separately distinguished.)

The following procedure was used: 25 mg of air-dried pulverized opium were rubbed thoroughly for 1 min in a mortar with 1 drop (0·05 ml) of sodium acetate-HCl buffer by Walpole (pH 3·9). Thereafter, 4·95 ml of the same buffer were added, stirring being continued for 3 min and the mixture filtered. The extinction of the filtrate was measured at 440 mμ wavelength, against the pure buffer, on a Jobin-Yvon 'Maroc' spectrophotometer, in 1 cm cells.

In the Figure the extinction readings obtained have been plotted against the year of production. From this diagram, a certain relationship between the extinction measured and the age of opium may be observed. Accord-

[1] LJ. GRLIĆ and J. PETRIČIĆ, Farm. Glas. *12*, 487 (1956); United Nations document ST/SOA/SER. K/48 (1957). – LJ. GRLIĆ, Acta pharm. jugosl. *7*, 199 (1957); United Nations documents ST/SOA/SER. K/54 (1957) and ST/SOA/SER. K/75 (1958).

ing to the results obtained, the type of opium examined shows on ageing a marked tendency towards increasing the yellow colour of the extract.

The nature of the water-soluble yellow pigments, which occur rather abundantly especially in old opium, does not seem to have been studied in detail so far. In order to explain the formation of the yellow pigment during the storage of opium, the intensity of the colour of a number of extracts belonging to different opium types has been compared with the results of the corresponding samples, obtained by means of our method of direct ultraviolet absorption spectrophotometry[1]. It has been observed that the intensely coloured samples of several types of opium were particularly distinguished by a high ratio E_{280}/E_{290}, obtained by our first extraction procedure, whereas most of the samples having only slightly coloured extracts exhibited rather low values of the same extinction ratio. As previously stated[1], this ratio is mainly affected by the quantity of meconic acid, being in reverse relation with the content of this constituent in opium. Consequently, a decreased content of meconic acid could be considered in general to be a characteristic of intensely coloured extracts of old opium.

In our opinion, an increased quantity of yellow pigments might be related to some extent to the parallel decrease of the meconic acid content in opium after longer storage. At present, we are not able to explain in detail the possible participation of the meconic acid molecule in the process of forming the yellow pigments. However, the γ-pyrone ring of meconic acid could possibly be considered as a component of the structure of a number of widely distributed natural pigments of the flavone group. As is known, the formation of these pigments in plants has not been explained so far in a satisfactory way.

It is obvious that various conditions of storage of opium (temperature, light, humidity) will affect to a certain degree the formation of the yellow colour observed. However, it should be mentioned that only slight differences in colour have been found between the extracts prepared from the surface and those from the inner part of the old opium cakes examined, which were exposed to light for more than 30 years.

Some preliminary examinations have shown that the age of some other types of opium (Iranian, Turkish) could also be established in a similar way. However, it is to be expected that various types of opium would give rather different results due to the differences in their content of meconic acid and other organic constituents. Therefore, such age determinations should be considered as reliable only if performed with opium of known origin, by means of a procedure tested and found suitable for the type concerned.

The procedure used in this paper is to be regarded as a preliminary one, even if applied only to the Macedonian opium. By calculating the results on a dry basis and by using a better method for the extraction (in order to avoid the absorption of pigments on the insoluble substances), one will undoubtedly obtain more exact and reliable results.

Acknowledgment. We are indebted to the Division of Narcotic Drugs of the United Nations and to the Institute for Pharmacognosy, Faculty of Pharmacy, Zagreb, for having kindly supplied us with a number of opium samples examined in this study.

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Institute for the Control of Drugs, Zagreb (Yugoslavia), January 28, 1959.

Résumé

L'intensité de la coloration jaune des extraits aqueux tamponnés d'opium macédonien est directement liée à l'âge de l'opium, ce qui permet d'évaluer approximativement l'année de la production de cet opium par un procédé colorimétrique très simple. L'accroissement de la teneur en pigments jaunes semble être accompagné d'une diminution parallèle de l'acide méconique au cours du vieillissement de l'opium.

Noise Induced Convulsions in Mice

In the past two decades considerable effort has been expended in attempts to define the physiological and/or psychological basis underlying audiogenic seizure susceptibility in animals. Much of the earlier literature through 1946 has been reviewed by FINGER[1]. Recently, BEVAN[2] has reviewed research from 1947 to 1954.

During the course of our studies on noise stress effects in animals[3] it was repeatedly observed that mice which were presumed seizure-resistant would enter into a violent running phase followed by a clonic or clonic-tonic convulsion when exposed to high intensity noise. This occurred more frequently with intense high frequency noise exposure than with intense low frequency noise. Despite the fact that there is no satisfactory explanation of the seizure triggering mechanism, a number of investigators adhere to a hypothesis advanced by MORGAN *et al.*[4] which maintains that the convulsion is the result of excessive auditory stimulation which effects overexcitation of auditory centers with a resultant spread into adjacent motor centers. Such an interpretation implies that the audiogenic-seizure may be a normal physiological response to a sound stimulus which exceeds the sensory threshold of the auditory center. If one accepts the possibility that sound induced convulsions are not a manifestation of some inherent physiological defect, it should be possible to use this abnormal behavior response as an endpoint for assessing an animal's limits of auditory sensitivity. It is with this in mind that the present study was initiated.

The animals used came from two laboratory strains of mongrel Swiss albino mice originally developed by FRINGS *et al.*[5]: one showing a high incidence of convulsions when exposed to noise (110 db, 10–20 kc) but no fatalities, and the other showing no convulsive response to noise. In the present investigation only the latter (seizure-resistant) mice were used.

Mice were selected at random from laboratory cages and exposed to one of three noise situations: (a) noise of moderate intensity in the high frequency range (110 db, 10–20 kc), (b) intense low frequency noise (135 db, 300–4800 cps), and (c) intense high frequency noise (132 db, 2–40 kc). Each mouse was exposed once for a duration of 1 min and the behavioral responses recorded especially with respect to the type of seizure elicited, i.e. running, clonic, or clonic-tonic.

[1] F. W. FINGER, Psychol. Bull. *44*, 201 (1947).

[2] W. BEVAN, Psychol. Bull. *42*, 473 (1955).

[3] These studies were aided in part by the Aero Medical Laboratory, Wright Air Development Center, Wright-Patterson Air Force Base under contract AF 33(616)-2505. This is paper No. 2349 in the Journal Series of the Pennsylvania Agricultural Experiment Station.

[4] C. T. MORGAN and H. WALDMAN, J. Comp. Psychol. *31*, 1 (1941).

[5] H. FRINGS and M. FRINGS, Behavior *5*, 305 (1955).