Oscillopolarographic Determination of Thalidomide

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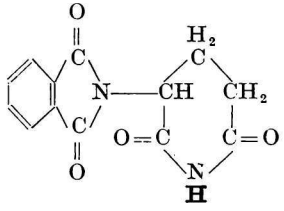
An oscillopolarographic method is described for the determination of *N*-phtalylglutamic acid imide (*Contergan*). The method involves recording of the curve of the function $dE/dt = f(E)$ in a supporting electrolyte composed of 0.1 M barbitone, 40 % methanol and 0.1 M-LiCl, where, in presence of thalidomide an irreversible cathodic incision is formed at the Q value of 0.66.

Thalidomide in concentration down to 2 μg/ml can be detected and quantitatively determined; presence of sulphates, nitrates, nitrites, chlorides or bromides caused no interference.

Polarographic determination of thalidomide was first reported by the author [1] working with a conventional D. C. polarograph and in present paper, D. C. polarographic technique is further extended to A. C. polarography.

The chemical formula for thalidomide was proposed by W. Kunz, H. Keller and H. Mückter [2] namely: *N*-phtalylglutamic acid imide:



thalidomide

The reduction persumably occurs at the carboxyl groups resulting in formation of free radicals.

Experimental

The work was carried out with P 576 Polaroscope, dropping mercury electrode and mercury pool as reference electrode. High purity thalidomide was supplied by Chemie Grünenthal GmbH. Barbitone (diethylbarbituric acid) was supplied by British Drug Houses, Ltd.

All chemicals were of analytical grade and demineralized water was used throughout the work.

Preparation of supporting electrolyte (S. E.)

4.6 g of barbitone were introduced into 250 ml volumetric flask followed by 100 ml of methanol and 25 ml 1 M-LiCl solution, shaken for a few times, 50 ml of water were

added, and shaken again, to complete the solution of barbitone, and made up to the mark with water.

At this stage the pH is 4.7 and S. E. is ready for the use.

Preparation of stock solution of thalidomide

100 mg of thalidomide were introduced into a 50 ml volumetric flask, 10 ml of dioxan were added and the flask was shaken until a clear solution was obtained and made up to mark with methanol. Standard solutions containing 40, 80, 160, 240, 320 μg/ml thalidomide were prepared by diluting the stock solution with methanol.

Oscillopolarographic measurements

One ml of each standard solution was introduced, in numerical order, into 5 flasks capacity of 10 ml and made up to the mark with S. E. The concentration of thalidomide in each flask, correspondingly, was 4, 8, 16, 24, 32 μg/ml. 5 ml from each flask were transferred into polarographic cell and the curve of the function $dE/dt = f(E)$ was recorded in usual way.

Typical curves are shown in Fig. 1 and Fig. 2.

The depths of incisions are found to be proportional to the concentration of thalidomide and the relationship is shown in the Fig. 3.

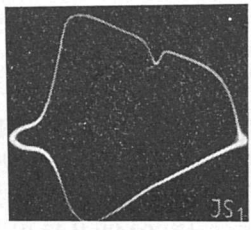


Fig. 1. $dE/dt = f(E)$ curve of thalidomide conc. 8 μg/ml.

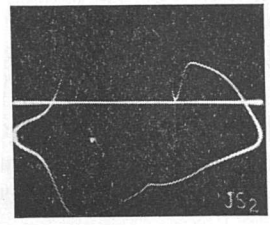


Fig. 2. $dE/dt = f(E)$ curve of thalidomide conc. 24 μg/ml.

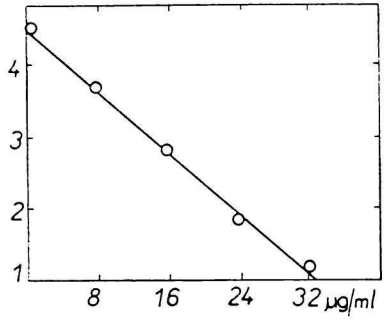


Fig. 3. Relation between concentration of Thalidomide and the depth of the incision.

Interferences

At pH above 6 no sharp incisions are formed, at pH 7.0 decomposition of thalidomide takes place (formation of a white precipitate). Addition of sulphates, nitrates, nitrites, bromides and all sedatives of barbituric group has no interference. Zinc causes interference due to formation of its own incision at the same potential as thalidomide.

OSCILOPOLAROGRAFICKÉ STANOVENIE THALIDOMIDU

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Thalidomid (*Contergan*, imid kyseliny *N*-ftalylglutamovej) dáva v základnom elektrolyte 0,1 м barbitalu, 0,1 м-LiCl a 40 % metanolu ireverzibilný katodický zárez (*Q* 0,66), ktorý možno použiť na kvantitatívne stanovenie skúmanej látky od koncentrácie 2 μg/ml.

ОСЦИЛЛОПОЛЯРОГРАФИЧЕСКОЕ ОПРЕДЕЛЕНИЕ ТАЛИДОМИДА

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Талидомид (*Контерган*, имид *N*-фталилглютамовой кислоты) дает на фоне 0,1 м-барбиталя, 0,1 м-LiCl, 40% метанола необратимый катодный зубец (*Q* 0,66), которым можно пользоваться для количественного определения начиная от концентрации 2 *мг/мл*.

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REFERENCES

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2. Kunz W., Keller H., Mückter H., *Arzneimittel-Forsch.* ***6,*** 8 (1956).

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