

# A NOTE ON THE DIFFERENTIATION BETWEEN DEXTRO- AND LAEVOPROPOXYPHENE

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A method is described for distinguishing between microgram quantities of the (+)- and (–)-isomers of propoxyphene.

DEXTROPROPOXYPHENE (Darvon), the  $\alpha$ -(+)-isomer of 4-dimethylamino-3-methyl-1,2-diphenyl-2-propionoxylbutane, came into use as an analgesic in 1957. Recently *laevopropoxyphene*, the (–)-isomer, has been marketed as an antitussive agent under the name of Letusin. Dextropropoxyphene is said to have an analgesic effect similar to that of codeine, and to be devoid of addictive properties. Internationally, it has been recommended for the same type of restriction as codeine, the *laevo*-isomer being free from control. In the United Kingdom, both isomers are subject to the provisions of Schedule 1 of the Dangerous Drugs Act.

Differentiation between these isomers might therefore become a matter of considerable forensic interest. Such distinction is not possible by ordinary analytical methods, but may, of course, be made polariscopically if sufficient material is available. On the microgram scale, use may be made of the method described by Clarke (1958) for the *N*-methylmorphinan analgesics. This depends on the fact that the racemic form of an alkaloid will usually form crystalline derivatives with certain reagents more easily than will either of the optical enantiomorphs. In the case of propoxyphene, gold chloride yields crystals almost at once with the racemic form, but only after standing for several hours with the (+)- and (–)-isomers.

*Practical procedure.* The test is carried out as follows, using the hanging microdrop technique of Clarke and Williams (1955). A microdrop of a solution of the test substance in 2*N* acetic acid is placed on a cover slip, and a microdrop of a 1 per cent solution of one known isomer (say, *laevopropoxyphene*), made by dissolving the base in 2*N* acetic acid, added. A microdrop of a 5 per cent solution of gold chloride is now added, and the cover slip sealed, inverted, and examined under the microscope in the usual way. If the test solution contained dextropropoxyphene, the drop will now contain both (+)- and (–)-isomers, and crystals of racemic propoxyphene aurichloride will quickly form; these appear as small, curved irregular needles, sometimes serrated, in bunches or branching chains. If, however, the unknown was *laevopropoxyphene*, the test drop will contain only this isomer, and crystals will not form for several hours, if at all. If they do, they are usually straight needles, considerably larger than those of the racemic form. Confirmation may be obtained by repeating the test, using dextropropoxyphene as the known isomer. A positive result may be obtained

**DIFFERENTIATION BETWEEN DEXTRO- AND LAEVOPROPOXYPHENE**  
with a 0·01 per cent solution of the test substance. As the volume of a microdrop is 0·1  $\mu$ l., the sensitivity of the test is thus 0·01  $\mu$ g.

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#### REFERENCES

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