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Apparent Oral Toxicity of 18-Crown-6 in Dogs

An apparent oral toxicity of 18-crown-6 (1,4,7,10,13,16-hexaoxacyclooctadecane) and sulfamonomethoxine (SMM)/18-crown-6 complex in dogs was investigated following the bioavailability study of SMM/18-crown-6 complex which the authors reported already. When 18-crown-6 or SMM/18-crown-6 complex was administered orally to healthy beagle dogs, the following symptoms appeared: a tremulous movement, a salivation and a paralysis of hind legs at 2—12 hr after administration. These symptoms disappeared at 24 hr after administration.

Keywords——18-crown-6; toxicity; sulfamonomethoxine/18-crown-6 complex; tremor; salivation; paralysis; beagle dogs

A toxicological investigation regarding crown ethers has been scarecely reported except dicyclohexyl-18-crown-6 of which toxicity was already reported by Pederson.[1]

The authors investigated already that 18-crown-6 (1,4,7,10,13,16-hexaoxacyclooctadecane) formed a complex with sulfamonomethoxine (SMM) in solid state[2] and that this complex was effective in increasing the bioavailability of SMM by oral administration in beagle dogs.[3]

The present paper is to report a special pharmacological effect, which was observed in the bioavailability study of SMM/18-crown-6 complex mentioned above.[3] Additionally, 18-crown-6 alone and the physical mixture of SMM and 18-crown-6 were examined to confirm this effect.

Healthy male beagle dogs weighing about 10 kg were used after washing out for one week or more and then fasting for 24 hr. In the case of SMM/18-crown-6 complex, six dogs were administered orally at a dose of 499.2 mg in a form of powder wrapped in two pieces of wefer.[3] Here, the dose corresponded to 199.2 mg of 18-crown-6 and 300 mg of SMM. In cases of 18-crown-6 alone and the physical mixture of SMM and 18-crown-6, two dogs each were administered in the same way as for the SMM/18-crown-6 complex with the following doses: 200 mg of 18-crown-6; 300 mg of SMM mixed with 200 mg of 18-crown-6.

As a result, the following symptoms appeared more or less in all the cases: a tremulous movement, a salivation and a paralysis of hind legs between 2—12 hr after the administration. These symptoms disappeared around 24 hr after the administration.

This result indicated that the toxicity of 18-crown-6 may be very strong, and further investigations should be made in order to know the mechanism of this kind of biological activity.

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