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Soft capsules formulated with ethanol; unexpected disulfiram-ethanol reaction after one dosage of Ciclosporin

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Objective

To report an unexpected disulfiram-ethanol reaction (DER) after exposure to ciclosporin formulated as a soft capsule containing ethanol endured by a patient under disulfiram treatment.

Table 1: Ingredients with known effect of Neoral-Sandimmun[®] 100 mg.

Molecule	Dose	Function
Ciclosporin	100 mg	Active principle
Ethanol	100 mg	Solvent
Propylene glycol	100 mg	Solvent
PEG-40 Hydrogenated Castor Oil	405 mg	Emulsifier/solubiliser

Reference; Summary of the product characteristics Neoral-Sandimmun[®] 100 mg

Reference

[1] Summary of product characteristics; Neoral-Sandimmun[®] 100 mg soft capsules. N.V. Novartis Pharma Vilvoorde (02/2020)

Case reports

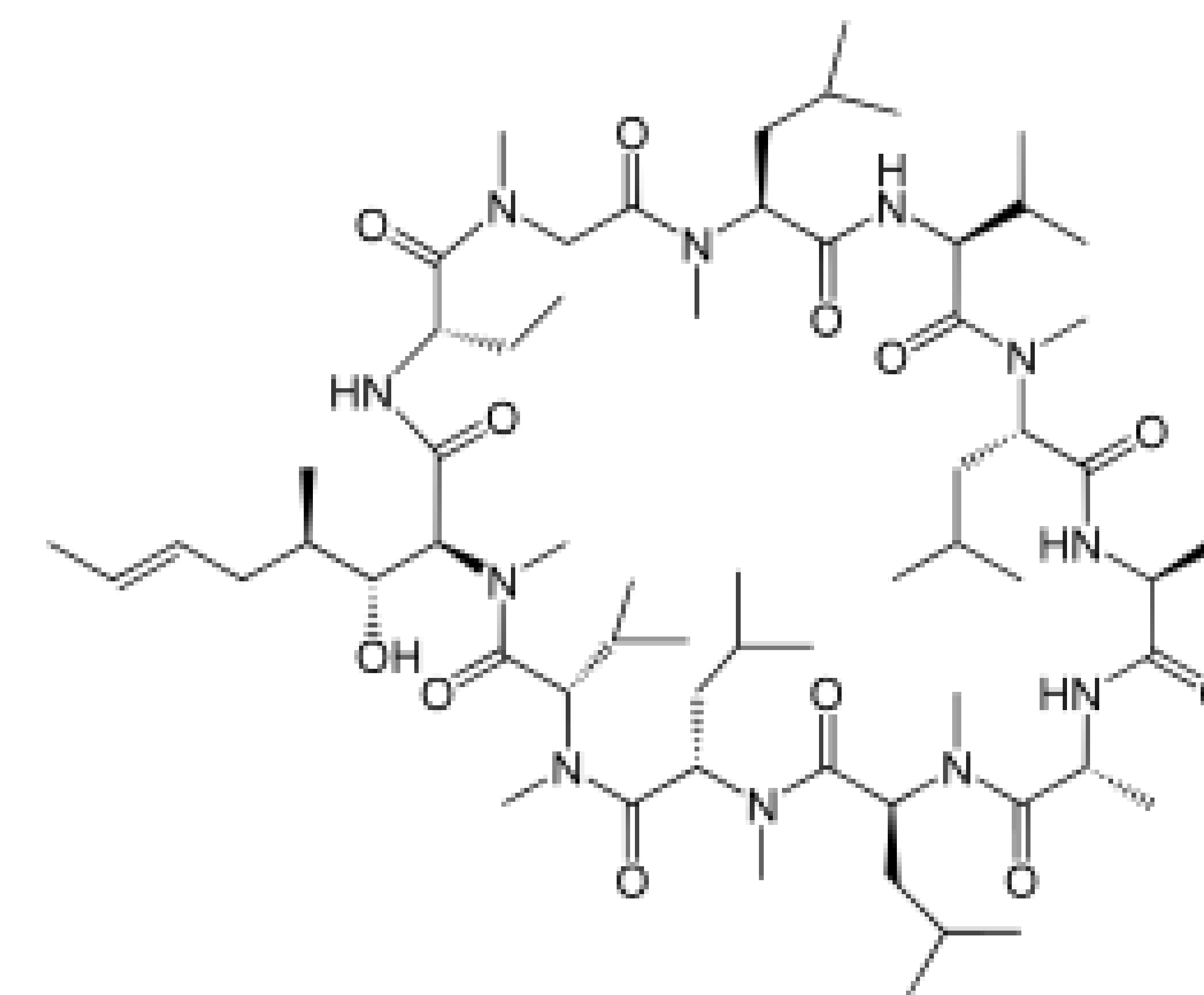
A patient, treated for ethanol dependence with disulfiram, was prescribed ciclosporin, commercialised as Neoral-Sandimmun[®], for a rheumatoid disease. After his first dosage, he presented a facial flushing with nausea and headache. The patient clearly recognised this symptoms as an initial stage of DER since he had suffered this before. His symptoms diminished gradually an hour later. Insecure about the origin of the ethanol responsible for his DER, he consulted the Poison Centre.

Discussion

As solid ciclosporin is practically insoluble in water, its biological availability is limited. To boost this biological availability, some ciclosporin medicines are formulated as a soft capsule containing a solution of ciclosporin in anhydrous ethanol. Accordingly, one dosage of Neoral-Sandimmun[®] has equal mass amounts of ciclosporin and ethanol which results in a 12 % (v/v) ethanol concentration in each soft capsule [1]. This was enough to provoke our patients initial stage of DER.

Conclusion

It is common for liquid medicines like syrups and droplets to contain ethanol. However some drugs like ciclosporin or some food supplement can also contain ethanol even though they are formulated as soft capsules. In this case the presence of ethanol in the soft capsules with ciclosporin provoked an unexpected initial stage of a DER. We would like to warn our colleagues, especially those working with alcoholics for this particularity.



Chemical structure of ciclosporin which is practically insoluble in water but freely soluble in anhydrous ethanol. (Ref: Ph. Eur. 7.0, 1678 (01/2009))

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