The crystal structure of the formamide solvate of (17b)-estra-1,3,5(10)-triene-3,17diol, C_{19}H_{27}NO_{3}

Experimental details

Hydrogen atoms were obtained geometrically and treated as riding on the parent atoms or were constrained in the locations during refinements.

Discussion

(17b)-estra-1,3,5(10)-triene-3,17diol (estradiol) (systematic name: (8R,9S,13S,14S,17S)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene-3,17-diol) is a member of the estrogen family of hormones, which was widespread used in hormonal replacement therapy for the treatment of postmenopausal symptoms and the protection against long-term consequences of estrogen deficiency (osteoporosis and cardiovascular disease) [3, 4]. Polymorphism, which is produced when compound crystallizes in various solid phases that differ in crystal packing [5–7]. Polymorphs can have different mechanical, thermal, physical, and chemical properties, such as compressibility, melting point, crystal habit, color, density, dissolution rate, and solubility. These can have a great influence on the bioavailability, hygroscopicity, stability, filtration, and tableting processes of pharmaceutical materials [8, 9]. Drug crystallization has been reported in many transdermal matrix systems [10, 11]. Due to the low solubility of estradiol [12], supersaturated patches containing high drug concentrations are often required for obtaining sufficient therapeutic efficiency. Recent work on the crystallization of estradiol in transdermal patches has revealed that the drug possibly crystallizes in more than one polymorphic form in the patch when stored for extended periods of time [13]. So it would thus appear important to anticipate conditions that give rise to crystallization, the

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Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

<table>
<thead>
<tr>
<th>Atom</th>
<th>x</th>
<th>y</th>
<th>z</th>
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Table 2 (continued)

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</table>

structure of the resulting crystals and, when necessary, possible ways of inhibiting crystallization. In the study on polymorphism of estradiol, we got the title solvate of the estradiol with formamide.

The asymmetric unit of the title contains two crystallographically independent molecules of estradiol and two
formamide solvent molecules. The estradiol and formamide molecules are hydrogen-bonded via N—H···O and O—H···O bonds. These connections lead to a hydrogen bonded framework. Bond lengths and angels of all moieties are in the expected ranges.

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References