

Polymorphs in hormonal therapy- A review

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Abstract- The pharma industry is always in the search of new, stable polymorphs. Even molecules used in hormone therapy due to their bulky size and bonding sites have become a major attraction now a days.

The estradiol is a major example in this study.

Keywords: Patents, Estradiol, polymorph, amorphous, crystalline

Introduction

Estradiol is a sex hormone found in women. This compound belongs to the category of steroids and is used as a drug in birth control pills. The other name of estradiol is 17β -estradiol or oestradiol. Estradiol is found to be 80 times as potent as estriol and 10 times more potent than estrone, in its estrogenic effects and is used in topical, injectable, oral, transdermal, and vaginal formulations. The estradiol molecule is linked to an alkyl group at C17 position to help the administration. Modifications at C17 position of this molecule (Fig 1) give rise to estradiol acetate (vaginal and oral applications), estradiol cypionate (injectable) and ethinyl estradiol (tablets) [1].

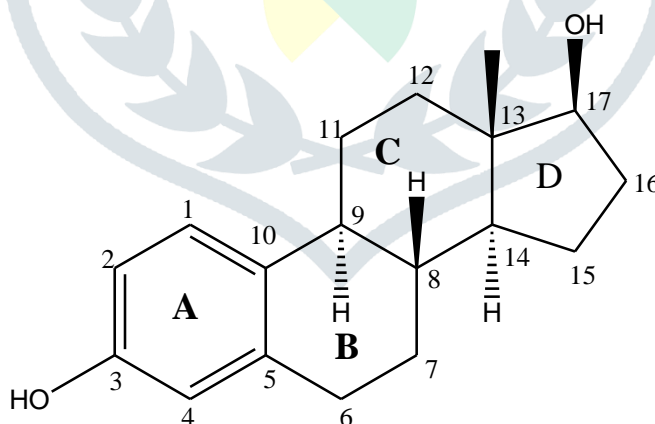


Fig 1 Structure of estradiol

The IUPAC name of estradiol is “1,3,5,(10)-estratriene-3,17-diol”. Its molecular formula is $C_{18}H_{24}O_2$ and molecular mass is 272.38.

Steroids are basically carbon compounds containing 4 rings joined to each other. Three are cyclohexane rings (A, B and C) and the other is cyclopentane ring (ring D). Steroids vary due to the functional groups attached to these rings. For example, ethinyl estradiol has acetylene attached to the ring at 17 position in the D ring [2,3].

Steroids are part of all plant, animals, fungi and human. All steroids are synthesized from sterols in cells like lanosterol (fungi and animals) and cycloartenol (plants) and are derived from triterpene squalene cyclization [4].

During liver metabolism the drugs have potent side effects so alternate routes of administration are looked upon. Transvaginal and transdermal are the most opted routes.

1.1 Polymorphism in estradiol

The literature survey reveals that not much work has been done on the polymorphism of estradiol. Varinakaval et al [5] reported 4 different crystal forms of estradiol (EA, EC, ED, EM), that were synthesized and characterized by thermal analysis, raman micro spectroscopy, optical microscopy and solid-state NMR. EA and EC were reported to have similar melting points. EA is hemihydrate having, moisture content of 3.5% while EC is an anhydrous form and did not show any weight loss in TGA. EM is a methanol solvate of Estradiol. ED is again an anhydrous form, which is prepared by melting EA and rapidly quenching the melt with liquid nitrogen.

Jeong Sook Park et al reported four crystal forms of Estradiol EM, ET, EP and EC prepared from methanol, acetone, ethanol, isopropanol [6]. These have been characterized by FT-IR spectra. The reported polymorphs are compared in Table 1.1.

Table 1.1 IR data of estradiol polymorphs

“Estradiol crystal Forms	Frequency (ν , cm^{-1})
EM	3471.24, 2919.70, 2862.81, 1609.31, 1499.38, 1450.21, 1283.39, 1250.61, 1072.23, 875.52, 816.71
ET	3447.13, 2935.13, 2838.70, 1585.20, 1498.42, 1449.24, 1282.43, 1250.61, 1055.84, 872.63, 819.60

EP	3450.03, 2935.13, 2862.81, 1611.23, 1497.45, 1453.10, 1283.39, 1249.65, 1056.80, 873.60, 819.60
EC	3448.10, 2935.1, 2862.81, 1609.31, 1498.42, 1449.24, 1282.43, 1249.65, 1055.84, 873.60, 819.60”

Conclusion: Estradiol clearly shows that how hormones have also been used for the polymorph study. The possibility of forming solvates and hydrates can be explored anytime. The formulation may be modified accordingly.

References:

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