Rapid and complete dissolution of the estetrol component into saliva is essential for efficient delivery of the component via sublingual, buccal or sublabial administration of the solid dosage unit. The inventors have unexpectedly found that the estetrol component is rapidly released and dispersed into saliva and absorbed through the mucosal lining of the oral cavity if it is present in the solid dosage unit in the form of very small particles.

The invention also provides a process of preparing the aforementioned solid dosage unit, said process comprising the steps of:

- providing estetrol particles containing at least 80 wt.% of an estetrol component selected from estetrol, estetrol esters and combinations thereof, said estetrol particles having a volume median diameter in the range of 2 µm to 50 µm;
- preparing a dry blend by mixing 1 part by weight of the estetrol particles with 2-1,000 parts by weight of one or more pharmaceutically acceptable excipients; and
- compressing the dry blend into a solid dosage unit.

Another aspect of the disclosure relates to the use of an estetrol component for the manufacture of a medicament in the form of a solid dosage unit as defined herein for medical treatment or for female hormone replacement therapy, wherein said solid dosage unit is to be administered sublingually, buccally or sublabially.

Another aspect of the disclosure relates to a method of female contraception, said method comprising sublingual, buccal or sublabial administration of a dosage unit as described herein.

BRIEF DESCRIPTION OF THE FIGURE

Figure 1 illustrates the manufacturing process flow chart used in Example 3.

DETAILED DESCRIPTION OF THE INVENTION

A first aspect of the invention relates to an orodispersible solid pharmaceutical dosage unit having a weight between 30 and 1,000 mg, said dosage unit consisting of:

- 0.1-25 wt.% of estetrol particles containing at least 80 wt.% of an estetrol component selected from estetrol, estetrol esters and combinations thereof; and
- 75-99.9 wt.% of one or more pharmaceutically acceptable ingredients;

the solid dosage unit comprising at least 100 µg of the estetrol component;

wherein the solid dosage unit can be obtained by a process comprising:

- providing estetrol particles containing at least 80 wt.% of an estetrol component selected from estetrol, estetrol esters and combinations thereof, said estetrol particles having a volume median diameter in the range of 2 µm to 50 µm;
- preparing a dry blend by mixing the estetrol particles with one or more pharmaceutically acceptable excipients; and

7. Dosage unit according to any one of the preceding claims, wherein the dosage unit contains 50-99.5 wt.% of filler selected from maltose, fructose, sucrose, lactose, glucose, galactose, trehalose, xylitol, sorbitol, erythritol, maltitol, mannitol, isomalt, microcrystalline cellulose, calcium salts and combinations thereof.

8. Dosage unit according to claim 7, wherein the dosage unit contains 50-99.5 wt.% of filler selected from lactose, xylitol, sorbitol, erythritol, mannitol, microcrystalline cellulose and combinations thereof.

9. Dosage unit according to claim 7 or 8, wherein the dosage unit contains at least 20 wt.% of sugar alcohol selected from mannitol, xylitol and combinations thereof.

10. Dosage unit according to any one of the preceding claims, wherein the dosage unit contains 0.1-20 wt.% of a disintegrating agent selected from modified starches, crosslinked polyvinyl pyrrolidone, crosslinked carmellose and combinations thereof.

11. Dosage unit according to any one of the preceding claims, wherein the dosage unit contains 0-60 wt.% of microcrystalline cellulose.

12. Dosage unit according to any one of the preceding claims, wherein the dosage unit contains 0.1-2 wt.% of lubricant selected from sodium stearyl fumarate, magnesium stearate, stearic acid, sodium lauryl sulfate, talc, polyethylene glycol, calcium stearate and mixtures thereof.

13. Use of an estetrol component for the manufacture of a medicament in the form of a solid dosage unit according to any one of claims 1-12 for medical treatment or for female hormone replacement therapy, wherein said solid dosage unit is to be administered sublingually, buccally or sublabially.

14. The use according to claim 13, wherein said solid dosage unit is to be administered once daily during a period of at least 1 week.