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# *Serenoa repens* as an Endocrine Disruptor in a 10-Year-Old Young Girl: A New Case Report

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**Key Words**
*S. repens* · Endocrine disruptor · Phytotherapy · Early menarche · Pediatric population

**Abstract**
*Serenoa repens*, commonly known as saw palmetto, is the sole species currently classified in the genus Serenoa. The plant is a low shrubby palm that is native of West Indies, and it grows in the coastal lands of North America and other European mediterranean countries. Its fruits contain high concentrations of fatty acids and phytosterols. *S. repens* extracts have been studied for the symptomatic treatment of benign prostatic hyperplasia. Recently, they have been proposed to treat androgenic alopecia and other hair disorders. We report a new case of hot flashes in a 10-year-old girl using a food supplement containing the extract of *S. repens* for the treatment of hirsutism. When the girl discontinued the treatment, the hot flashes stopped. A 'rechallenge' of the supplement was tried and symptoms reappeared. About 4 months after starting therapy, the girl experienced menarche. Exposure to the plant-derived product could be responsible for the appearance of menarche. In our opinion, use of phytotherapeutic agents in pediatric patients should be associated to a better evaluation of benefit/risk profile taking in account the physiological changes that occurs at different ages in this subgroup of population. 

## Introduction

The use of medicinal plant products to keep and promote health supplements comes from a long tradition. In most of the countries, plant-derived products are not regulated as medicinal products and are marketed as food supplements. Both in Europe and the United States as well as in other countries, regulation of food supplements does not require proof of efficacy and particular limitations of use are not established. The extracts of saw palmetto fruits, highly rich in fatty acids and phytosterols, have been the subject of intensive preclinical and clinical research assessing their potential efficacy as symptomatic treatment for benign prostatic hyperplasia [1]. In fact, they share the same mechanism of action with finasteride acting as dual inhibitor of prostatic 5α-reductase isoenzyme. Also, it is thought to decrease dihydrotestosterone uptake by hair follicle and to inhibit the binding of dihydrotestosterone to androgenetic receptors [2]. Recently, extracts of this plant were also indicated, because of their effects on 5α-reductase enzyme activity, to treat androgenic alopecia and other hair disorders in alternative to conventional treatments [3]. The extracts of this plant are generally well tolerated in adult males; however, more attention is needed about its use in children because in a previous case, a 11-year-old girl treated for 'telogen effluvium' with *Serenoa repens* extracts experienced hot flash-


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es with hypermenorrhea and polymenorrhea [4]. Herein, we describe a new case of a young girl experiencing similar symptoms after *S. repens* intake.

## Case Report

We observed the case of SD, a 10-year-old Caucasian girl, before menarche, weighing 44 kg and with a height of 142 cm (body mass index (BMI) 21.52) from Calabria in southern Italy. She was affected by hirsutism for 2 months. For this problem, a dermatologist prescribed oral administration of capsules containing *S. repens* extract. In particular, each capsule contained 320 mg of a standardized oily extract of the fruits of *S. repens*. The constituents of the extract were 85–95% of fatty acids (lauric, myristic, caprylic, capric, palmitic, oleic, linoleic and linolenic acids), methyl and ethyl ester fatty acids (0.01–0.15%), saturated and unsaturated long chain alcohols, 0.25–0.50% of total sterols and 0.15–0.35% of β-sitosterol. The young girl was not taking other drugs or food supplements. She was administered one capsule once a day containing *S. repens* for a period of 3 months with an interval of 8 days after every 30 days of treatment. During the third month of treatment, the girl experienced hot flashes several times during a day and a rapid weight gain: before therapy, the girl was 37 kg with a height of 142 cm (BMI 18.35). On the advice of her pediatrician, she stopped the treatment and the hot flashes disappeared in 14 days. Following the pediatrician's advice, therapy was reassumed ('rechallenge') and symptoms reappeared in 4 days. Therefore, the treatment was definitely suspended. About 4 months (113 days) after the start of therapy and 25 days from the cessation of the intake of the food supplement, the girl experienced menarche with polymenorrhea (bleeding duration: 17 days) and hypermenorrhea. The irregularities of menstruation prolonged for 1 month after menarche. The girl was visited by a gynecologist. The pelvic echography showed a normal uterus and immature ovaries for her age. The hormonal status of the girl was not investigated with blood tests.

## Discussion

The age of our young patient (10 years) could be congruous with prepubertal/pubertal stage. It is not possible to establish whether the appearance of menarche was caused by intake of the *S. repens* extract; however, an anticipation of menarche cannot be excluded. To investigate the relationship of causality, we used the Naranjo probability scale obtaining a score of 6, indicating that the relationship between hot flashes and administration of the therapy as probable [5]. *S. repens* products are commonly well tolerated, although mild (i.e. rhinitis, nausea, abdominal pain, diarrhea, headache, dermatitis, fatigue and decreased libido) [4], or severe adverse events such as hepatitis and pancreatitis have been reported; in addition, cases of intraoperative hemorrhage and coagulopathy associated with the use of this plant have been also described (table 1). An explanation of the mechanism by which *S. repens* could cause hot flashes and vasomotor symptoms can be attempted. In postpubertal girls, such symptoms could be related to its antiestrogenic activity and to the increase of available sex hormone-binding globulin [4]. Changes in sensitivity of body's thermostat (hypothalamus), that becomes more sensitive to slight changes in body temperature, are considered the triggering mechanism of hot flashes. This function is influenced either by estrogens or by gonadotropin plasma levels [6]. If these are the most common causes in woman during menopause, they are insufficient to explain hot flashes in a prepubertal patient. In our case, since estrogenic plasma levels are low in prepubertal girls, it could be hypothesized that vasomotor symptoms are related to the alteration of gonadotropin plasma levels which are induced by *S. repens* intake.

**Table 1.** Serious reactions reported after *S. repens* intake

| Serious adverse reactions | Authors of the case report |
|---|---|
| Hepatitis | Lapi F, et al: Acute liver damage due to Serenoa repens: a case report. Br J Clin Pharmacol 2010. |
| Intraoperative hemorrhage | Cheema P, et al: Intraoperative haemorrhage associated with the use of extract of Saw Palmetto herb: a case report and review of literature. J Intern Med 2001. |
| Coagulopathy | Villanueva S, et al: Coagulopathy associated by saw palmetto: a case report. Bol Asoc Med P R 2009. |
| Pancreatitis | Wargo KA, et al: A possible case of saw palmetto-induced pancreatitis. South Med J 2010. |
| Hepatitis and pancreatitis | Jibrin I, et al: Saw palmetto-induced pancreatitis. South Med J 2006. |

It seems that the androgens could have a functional role in regulating puberty timing in girls. In particular, it has been observed that an association between higher levels of adrenal androgens in girls of prepubertal age with earlier menarche. Moreover, it has been suggested that higher levels of these hormones in children experiencing rapid weight gain may have a role in developmental pathways leading to earlier sexual maturation [7]. Several studies have demonstrated that obese girls are more likely to have earlier menarche; thus, central puberty is eventually initiated and obese girls progress more rapidly to the onset of mensuration [8]. These findings could ex-

plain what occurred in the girl described in our case, even if the girl experienced a dramatic increase in BMI (+3.2) in <4 months; however, the treatment period with *S. repens* has been much too short to produce obesity.

## Conclusions

To date, scientific literature provided only limited data on the efficacy and safety of *S. repens*-containing products administered to women and children. Health-care practitioners, in the light of the antiandrogenic effects of *S. repens* influencing physiological endocrine activity, should exercise caution in the use of this plant, in particular, in prepubertal age. *S. repens* could have complex effects on the endocrine system by acting as endocrine disruptor.

## Disclosure Statement

The authors have no conflicts of interest to declare.

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