Phytotherapy and intraoperative floppy iris syndrome: the implications

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Introduction

Intraoperative floppy iris syndrome (IFIS) was first recognised and described in 2005.^{1,2} It is characterised by poor pupil dilatation, billowing of iris stroma, iris prolapse through corneal incisions, and progressive intraoperative pupillary constriction.¹ The incidence of IFIS can vary, representing between 2–3% of the entire cataract population, but it can be >50% in patients taking Tamsulosin—a selective α_1 -adrenergic blocker, compared to other non-selective α -adrenergic blockers such as Alfuzosin, Doxazosin, and Terazosin.^{1,3,4}

Alpha-adrenergic antagonists are commonly used in the treatment of benign prostate hyperplasia (BPH).⁵ The last few years have seen a rise in the use of herbal treatment for BPH, with Saw Palmetto being the most common herbal alternative treatment. Saw Palmetto has been shown to have an α -adrenergic effect.⁶ As herbal medications and supplements are often not considered as medications by the patients and thus omitted during history taking unless directly prompted to do so, it is important for the surgeon to be aware of all medications and supplements that could potential cause IFIS.⁷

Aim

To assist in this process, we examined the contents, names, and indications of commonly encountered herbal remedies containing α -adrenergic blockers in Europe, United States, and Australia.

Materials and methods

We performed an internet-based study looking at all pharmacy and health food store chains of major European countries, United States,

Australia, and New Zealand. The European sites used were from the United Kingdom, France, Germany, Spain, and Greece.

Results

The names of the herbal remedies, indications for their use, and their contents and active ingredients are summarised in Tables 1 and 2.

The main indication for these herbal remedies was BPH followed by hair loss, reproductive health and fertility, migraine, and their use as a herbal aphrodisiac. The commonest active ingredient was Saw Palmetto followed by Pygeum. Saw Palmetto concentration ranged between 160 mg and 4 g. Pygeum concentration ranged between 5 and 100 mg.

Discussion

In recent years, herbal remedies are becoming increasingly popular for the treatment of medical conditions including BPH. In Germany and other European countries, herbal medication has become the first-line treatment for mild to moderate symptoms of BPH.⁶

The most common herbal medication used for BPH is American dwarf palm, also known as *Serenoa repens* or Saw Palmetto. Its mode of action is complex as it is thought that it exerts an effect through various pathways. It has been reported that it bears an α -adrenergic antagonistic effect and can potentially increase the risk of IFIS.^{6–8} In 2002, a survey examining the use of complementary and alternative medication found that, in the United States, 18.9% of age-adjusted adults use complementary products, and of these, 5.8% use Saw Palmetto.⁹

Rye grass pollen extract commonly known with its commercial name Cernilton (also as ProstaBrit in the United Kingdom) relaxes urethral smooth muscle tone and increases bladder muscle contraction. It has been shown to have an anti- α -adrenergic action.¹⁰

Table 1 Herbal remedies containing α -adrenergic blockers in Europe

Product	Doses	Indication
<i>United Kingdom</i>		
Saw Palmetto capsules	80, 320, and 450 mg	Symptoms of BPH
Multivitamins	Contains: Saw Palmetto (160 mg)	Reproductive health and fertility
Protace (WellMan)		
Multivitamins	Contains: Saw Palmetto (160 mg)	Hair loss+nutritional supplement
Nanogen (men over 40+)		
Multivitamins	Contains: Saw Palmetto (160 mg)	Hair loss+nutritional supplement
Nanogen (men over 20+)		
Multivitamins	Contains: Saw Palmetto extract and Pygeum extract	Symptoms of BPH
Formula 600 Plus for men (PSC)		
<i>Germany</i>		
Saw Palmetto capsules	120, 540, 550, 100, and 2500 mg	Symptoms of benign prostate hyperplasia Reproductive health and fertility Hair loss
<i>Pygeum africanum</i> capsules	100 mg	Symptoms of BPH
Multivitamins	Contains: Pygeum extract	Symptoms of BPH
T-Bomb II (MHP)		
Multivitamins	Contains: Pygeum extract	Symptoms of BPH
Prostate Health (Biovea)		
Multivitamin	Contains: Saw Palmetto and Pygeum extract	Symptoms of BPH
Saw Palmetto Complex (Newton-Everett Biotech)		
<i>France</i>		
Saw Palmetto capsules	160, 295, 300, 320, and 1010 mg	Symptoms of BPH Hair loss
<i>Pygeum</i> capsules	100 and 250 mg	Symptoms of BPH
Multivitamin	Contains: Saw Palmetto (60 mg)	Symptoms of BPH
Prostata' Home (Dieti Naura Co.)	Contains: Saw Palmetto and Pygeum extract	
Sabal/Pygeum (Gph Diffusion)		
<i>Spain</i>		
Saw Palmetto capsules	300 and 550 mg	Symptoms of benign prostate hyperplasia Hirsutism Herbal aphrodisiac Hair loss
Multivitamins	Multiple ingredients including: Saw Palmetto	
Lambdapil (ISDIN)		
Combination therapy	Multiple ingredients including: Saw Palmetto	Symptoms of BPH
Prosor (Soria Natural)		
Combination therapy	Multiple ingredients including: Saw Palmetto (30 mg)	Symptoms of BPH
Prosavital (Health Aid)	Pygeum (5 mg)	
Combination therapy	Multiple ingredients including: Saw Palmetto (80 mg)	Symptoms of BPH
Saw Palmetto (Nature's Bounty)	Pygeum (10 mg)	
<i>Greece</i>		
Saw Palmetto capsules	300 and 320 mg	Symptoms of BPH

Pygeum africanum, the extract of the African prune tree is used to treat lower urinary tract symptoms. It can be used alone or in combination with Saw Palmetto.¹¹ Pygeum improves the symptoms of BPH through its effects on bladder contractility, anti-inflammatory action, inhibition of fibroblast production, and endocrine effect, but no effect on the α -adrenergic receptors has been reported.¹¹

An interesting and slightly surprising fact of our study is that the indications for the use of these α_1 -antagonistic herbal supplements are very variable. This may be due to the use of some of these supplements as traditional remedies or the more 'holistic' treatment perception associated with herbal remedies. Although Saw Palmetto and other herbal remedies have been used for a variety of indications separately, their combination, that is, Saw Palmetto with Pygeum was solely used for the treatment of BPH.

Plant extracts are more complex than synthetic compounds and exert their therapeutic action often

through more than one pathway and their mode of action is often elusive. Phytotherapy is becoming increasingly popular to treat an array of medical conditions, and the possibility of a patient self-medicating with a substance that can affect iris tone and cause IFIS is ever increasing.

IFIS has been associated with an increased risk of intraoperative complications during intraocular surgery such as iris prolapse through surgical wounds, increasing pupillary miosis during surgery, iris trauma, and an increased risk of posterior capsule rupture with vitreous loss.^{12,13} Chang *et al*¹ reported an increased risk of posterior capsular rupture in their IFIS group patients recording a rate of 12%. Recognition of the risk factors associated with IFIS allows the surgeon to prepare pre-operatively and reduce the risk of unexpected intraoperative surprises. Predicting which patients are at risk of IFIS is crucial at pre-assessment and at the pre-operative ward round.

Table 2 Herbal remedies containing α -adrenergic blockers in United States, Australia and New Zealand

Product	Doses	Indication
<i>United States</i>		
Saw Palmetto capsules	160, 200, 320, 350, 450, 500, 550, 585, 600, and 900 mg	Symptoms of BPH Upper respiratory tract symptoms Pelvic pain syndrome Headaches (including migraine) Sedative Herbal aphrodisiac Hair loss in men Symptoms of BPH
Multivitamins	Contains: Saw Palmetto (320 mg)	Symptoms of BPH
The prostate formula (Real health)		
Combination therapy	Contains: Saw Palmetto (320 mg) Pygeum (100 mg)	Symptoms of BPH
Solaray		
Combination therapy	Contains: Saw Palmetto (320 mg) Pygeum (100 mg)	Symptoms of BPH
Country Life		
Combination therapy	Contains: Saw Palmetto (320 mg)	Symptoms of BPH
Saw Palmetto and nettle with pumpkin (Solaray)		
Combination therapy	Contains: Saw Palmetto (100 mg) Pygeum (60 mg)	Symptoms of BPH
Super Saw Palmetto plus Pygeum (Action Labs)		
Combination therapy	Contains: Saw Palmetto (320 mg) B-Sitosterol (120 mg from Pygeum extract)	Symptoms of BPH
Saw Palmetto Complex with Lycopene (Nutricology)		
<i>Australia</i>		
Saw Palmetto capsules	1.6 and 3.2 g	Symptoms of BPH
Combination therapy	Contains: Saw Palmetto (1.6 g)	Symptoms of BPH
Prostate Health Formula (Blackmores)		
Combination therapy	Contains: Saw Palmetto Pygeum	Symptoms of BPH
Pros-P10x		
<i>New Zealand</i>		
Saw Palmetto capsules	160, 400, and 550 mg	Symptoms of BPH
Multivitamin—Prostate Complete (Nutra-Life)	Contains: Saw Palmetto (4 g)	Herbal aphrodisiac
Combination therapy	Contains: Saw Palmetto (320 mg) Pygeum	Symptoms of BPH
Saw Palmetto and Pygeum extract (Country Life)		
Combination therapy—Ultra natural Prostate (LifeExtension)	Contains: Saw Palmetto (320 mg) Pygeum (100 mg)	Symptoms of BPH

The association between IFIS and the use of α -antagonists is established. The consensus is that urologists should not change their prescribing habits, but should consider informing the patient's ophthalmologist especially if the patient has been diagnosed with cataracts or cataract surgery has been planned.¹⁴ Studies examining the effect of herbal medication on iris tone are limited, but there has been a suggested risk of IFIS through an α -adrenergic pathway, similar to that of Tamsulosin.^{6–8} To our knowledge, no study has examined the effect of herbal medications cessation to iris tone, but one would assume that effect to be similar to that of Tamsulosin cessation.⁹ Adopting an awareness policy similar to that for pharmaceutical medication should suffice.

A point to stress is that our study highlights a broad use of α -adrenergic antagonistic herbal supplements from BPH to hair and used as a natural aphrodisiac. With the ever growing population's life expectancy, the need for efficient and complication-free cataract surgery will continue to grow. The anticipation and prediction of IFIS risk can help the operating surgeon minimise the intraoperative complications and lead to safer surgery with increasingly successful outcomes. Patients often do not consider herbal remedies and vitamins to be

medication, and therefore fail to mention them unless directly prompted to do so. Our recommendation is that patients should be directly asked about the use of alternative therapies for recreation or medicinal purposes, and for the clinician or pre-assessment nurse to be aware of specific formulations that are or could potentially be associated with increased surgical risk and possibly a compromised surgical outcome.

Conflict of interest

The authors declare no conflict of interest.

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