Serenoa repens (saw palmetto): a systematic review of adverse events
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CRD summary
The authors concluded that available data suggested that Serenoa repens (Saw Palmetto) was well tolerated by most users and was not associated with serious adverse events; there was no evidence of drug interactions. Overall, this was a well-conducted review and the authors’ conclusions are likely to be reliable.

Authors' objectives
To evaluate the safety of monopreparations of Serenoa repens (S. repens) (saw palmetto).

Searching
MEDLINE, AMED, EMBASE, CINAHL and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from inception to February 2008 for studies in any language. Search terms were reported. Reference lists of identified papers were screened. The authors’ own department’s files were searched. Reporting schemes of Australia, Germany, USA (Food and Drug Administration) and UK were used to retrieve additional data. World Health Organisation was contacted. Twenty-four manufacturer/distributors of S. repens and four herbalist organisations were contacted.

Study selection
Inclusion criteria appeared to be any study or source of data about reports of adverse events in people treated with monopreparations of S. repens. Studies of combined preparations of S. repens were excluded.

Data sources included randomised controlled trials (RCTs), non-randomised controlled trials, uncontrolled trials, case reports, case series, surveys and post-marketing surveillance studies. Participants were mostly men diagnosed with benign prostatic hypertrophy, men with stages I-II prostatic adenoma and lower urinary tract symptoms. A minority of studies were in healthy volunteers or other medical conditions. Where reported, duration of S. repens treatment was most commonly six months or less; in some studies treatment was for five years. Where reported, studies used different S. repens preparations; the most commonly used preparation was Permixon. All except one study used oral S. repens in daily doses that ranged from 100mg to 480mg. Control treatments, where these existed, included finasteride, tamsulosin, alfuzosin, herbal combinations and placebo.

Studies were selected by one reviewer and selection was verified by a second reviewer. Disagreements were resolved through discussion between co-reviewers.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Data on adverse events were extracted by one reviewer using a predesigned form and verified by a second reviewer. Disagreements were resolved through discussion. One reviewer extracted data from papers not in English or German.

Methods of synthesis
The studies were grouped by study design and combined in a narrative synthesis.

Results of the review
Forty studies were included: 14 placebo-controlled randomised clinical trials (RCTs, n=1,557); 12 comparative RCTs (n=3,125); four non-randomised clinical trials (n=179); six uncontrolled trials (n=1,034); and four case reports or series (n=5). Data from National Reporting Schemes based in UK, Germany, Australia, USA and at WHO, manufacturers and one herbalist organisation were included.

Adverse events reported in placebo-controlled RCTs (14 RCTs, n=1,557) included diarrhoea and other gastrointestinal
problems (n=18), headache (n=6), fatigue (n=6), common cold (n=3), gastrointestinal bleeding (n=3), urinary problems (n=2), nausea (n=1) and vomiting and vertigo (n=1).

Adverse events reported in non-placebo-controlled RCTs (12 RCTs, n=3,125) included gastralgia, abdominal discomfort, hypertension, decreased libido, impotence, ejaculation disorder, gastrointestinal disorder, rhinitis, headache, fatigue, dizziness and skin disorders.

Results for other sources of data were reported.

More serious adverse events including death and cerebral haemorrhage were reported in isolated case reports or as data from spontaneous reporting schemes; the causality of the relationship to S. repens was unclear. No drug interactions were reported.

**Authors’ conclusions**
Available data suggested that S. repens was well tolerated by most users and was not associated with serious adverse events. Most adverse events are mild, infrequent and easily reversible. There was no evidence of drug interactions.

**CRD commentary**
The review question was clearly stated and inclusion criteria were defined; broad criteria for study design and participants were appropriate given that the review evaluated safety. The search was extensive and no language restrictions were applied. Methods were used to minimise reviewer errors and bias in study selection and data extraction. Reasons for not formally assessing study quality were discussed. Although some limitations of the evidence were discussed (including a lack of information about participants and inability to attribute causality to reports in many data sets), further discussion of validity of reported data may have been helpful. Suitable methods were used to group studies. Use of a narrative synthesis was appropriate given the diversity among studies. Most participants whose medical condition was specified were men with prostate symptoms. Little information was provided about participants from the larger data collections in databases. These potentially limited the generalisability of findings. Overall, this was a well-conducted review and the authors’ conclusions are likely to be reliable.

**Implications of the review for practice and research**
Practice: The authors did not state any implications for practice.

Research: The authors stated that higher-quality reports of adverse events were required to improve future assessments of safety.

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