

CRATAEVA AND EQUISETUM REDUCE URINARY INCONTINENCE SYMPTOMS

INTRODUCTION

Incontinence is a common condition in Australia and throughout the world, affecting from 12 per cent of 18 year old women and up to 50 per cent of women in their 70s¹.

Current drug therapy includes anticholinergics (with antispasmodic effects, such as oxybutynin), smooth muscle relaxants (antispasmodics), tricyclic antidepressants (such as imipramine), alpha-adrenergic antagonists, alpha-adrenergic agonists (such as phenylpropanolamine), prostaglandin synthesis inhibitors, calcium channel blockers and others²⁻⁵. Unfortunately, most drug treatments are associated with unpleasant side effects, and this impacts on patient compliance²⁻⁵.

Natural therapies are also being investigated for this condition⁶⁻⁹. In Ayurveda (traditional Hindu science of medicine), the herb *Crataeva nurvala* is a drug highly regarded for its use in the management of uropathies¹⁰. Western traditional treatments recommend the use of the herb horsetail, *Equisetum arvense*¹¹.

A review of research indicated treatment with *Crataeva* (equivalent to 25 grams twice daily over 20 to 40 days) was shown to relieve urinary incontinence, pain and retention of urine in 30 men with benign prostatic hyperplasia¹². *Crataeva* also showed beneficial effects on neurogenic bladder and post-prostatectomy atony of the bladder.

In addition, cystometric studies indicate that *Crataeva* significantly decreased residual urine volume and normalised the tone of the urinary bladder¹². The herb has also been shown to be of benefit for the treatment of urinary calculi and infection¹²⁻¹⁹.

Horsetail is documented in traditional texts as a genito-urinary astringent beneficial in the treatment of urinary incontinence and enuresis of children¹¹. It has been shown clinically to have anti-inflammatory, anti-bacterial and anti-lithogenic effects^{11, 20-24}.

This paper reports the results of a pilot study investigating the efficacy of a tablet preparation containing these drugs in relieving symptoms of urinary incontinence. It also provides a discussion of possible mechanisms of action of these drugs.

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PATIENTS AND METHODS

Eight women experiencing symptoms of urge incontinence and/or stress incontinence on a regular basis were recruited through newspaper advertisements. All women met the following criteria:

- Had not undergone recent surgery, particularly hysterectomy or prolapse repair, within the last 12 months.
- Did not have any serious health conditions such as diabetes mellitus, heart disease, pancreatic disease, hepatic disease or chronic inflammatory conditions.
- Were not currently being treated for psychotic disturbances.
- Did not use any medicine for incontinence symptoms in the last month prior to commencement of the study.

The treatment protocol consisted of two tablets twice daily (equivalent to 12g *Crataeva* and 6g *Equisetum* daily) over a period of 12 weeks. The efficacy of the treatment was assessed using the short versions of the Incontinence Impact Questionnaire (IIQ) and the Urogenital Distress Inventory (UDI) prior to commencing treatment (month 0) and each month thereafter (months 1, 2 and 3).

The short version (six questions) of the IIQ assesses the impact of incontinence on daily activities, such as household chores, physical activity and social activities. The questions in the UDI relate specifically to the physical aspects of incontinence. All questions are rated on a scale of 0-3 (0=not bothered, 1=slightly bothered, 2=moderately bothered, 3=extremely bothered). Both questionnaires are standardised disease specific questionnaires used to detect bothersome incontinence in older people²⁵. The results of these questionnaires were analysed using the paired T-Test.

The tablets were manufactured in accordance with the GMP guidelines by a TGA approved manufacturing site. They contained the herbs *C. nurvala* bark and *E. arvense* leaf and the minerals Magnesium phosphate and Calcium phosphate. The study was conducted according to the TGA's *Guidelines for Good Clinical Research Practice (GCRP) in Australia*. The Australian College of Natural Medicine Ethics Committee approved the study. The interviews were conducted at the Naturopathic Clinic at the Australian College of Natural Medicine, Brisbane.

RESULTS

The study group consisted of 8 women. Seven of the participants were aged between 54 and 65, with one participant being 20 years of age. The average age of the study group was 50 years. Six of the participants had given birth to at least two children, while two participants had not had children.

The effectiveness of this treatment on the physical symptoms is presented in Table 1 and Figure 1. Prior to treatment, 80 per cent of the participants reported that they were bothered by leakage related to activity. This was reduced to 40 per cent after 3 months of treatment (Figure 1). Similar responses were observed for leakage due to urgency (60-35 per cent), frequent urination reduced (70-48 per cent), and difficulty emptying bladder (50-25 per cent). Prior to treatment, 50 per cent of participants experienced pain or discomfort prior to treatment, but none reported these symptoms after 2 months of treatment. There was a 25 per cent reduction in the number of women responding to small amounts of leakage (75-50 per cent) after treatment.

Analysis (paired T-Test) of the data indicated that there was a

Table 1. Urogenital Distress Inventory.

Do you experience, and if so, how much are you bothered by:	Month		
	1	2	3
• Frequent urination	0.040	0.024	0.013
• Leakage due to feeling or urgency	0.052	0.024	0.024
• Leakage due to activity, coughing, sneezing	0.086	0.009	0.031
• Small amounts of leakage (drops)	0.178	0.145	0.091
• Difficulty emptying bladder	0.025	0.025	0.052
• Pain or discomfort in lower abdominal/genital area	0.366	0.025	0.025

Paired T-Test p<0.05

significant positive change in the perceptions of frequency of urination after a month of treatment (p=0.040), and this continued in a gradual manner over the duration of the study (p=0.24 at 2 months, p=0.013 at 3 months). There was a significant positive change in perceptions regarding leakage relating to urgency (p=0.024), leakage due to activity (p=0.031), and difficulty emptying bladder (p=0.052) after 3 months of treatment. Positive effects were also seen after the first initial month of treatment.

There was a positive trend in the responses regarding the small amounts of leakage during the study but these were not significant. A significant positive response in relation to pain or discomfort in the lower abdomen or lower region (p=0.025) was also observed after 2 months of treatment.

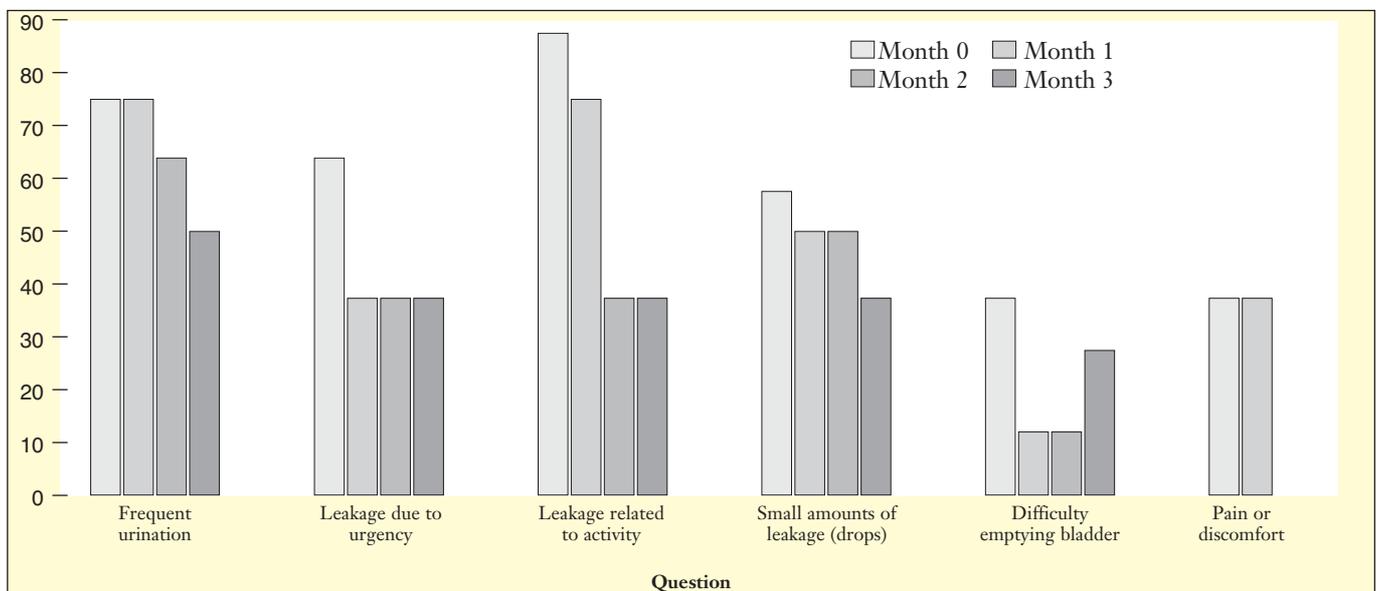
The responses to the IIQ are presented in Table 2 and Figure 2. The results indicated that participants felt that incontinence had a significant negative impact on their quality of life, as assessed by a range of 50-70 per cent “bothered score” for the 7 parameters of the IIQ (Figure 2). This was reduced significantly (to a range of 10-25 per cent) for all parameters, except the question regarding physical recreation, in which there was little variation between month 0 and month 3.

Analysis (paired T-test) of the data showed that there was an improvement in the perception of the effect of incontinence on lifestyle and social activities, indicated by positive changes in response to social activities (p=0.04), entertainment activities (p=0.017), emotional health (p=0.025) and travel greater than 30 minutes from home (p=0.052), feeling frustrated (p=0.007) after 3 months of treatment. There was no change in the responses regarding household chores or physical recreation (Table 2).

DISCUSSION

The results from this study indicate a significant (at p<0.05) improvement in the control of leakage (due to urgency and

Figure 1. Percentage of “bothered” (1, 2 or 3) responses.



physical activity), bladder emptying and pain or discomfort after three months of treatment. These results are supported by earlier studies indicating that treatment with *Crataeva* relieved incontinence, pain and retention of urine^{8,12}.

Acetylcholine is the primary excitatory neurotransmitter involved in bladder emptying. Certain drugs commonly prescribed for urinary incontinence, such as oxybutynin hydrochloride, inhibit the muscarinic action of acetylcholine on smooth muscle, producing a direct antispasmodic action. That is, they relax the detrusor muscle^{5,26}. These medications also produce unwanted anticholinergic effects, such as dry mouth, blurred vision and constipation⁴. There are currently no medications that specifically target incontinence symptoms without having side effects elsewhere in the body.

The mechanisms whereby these herbal drugs exert these effects are unknown. It is thought that the primary active ingredients present in both *Crataeva* and *Equisetum* are the saponins and plant sterols. *Crataeva* contains flavonoids, glucosinolates and the plant sterol, lupeol, while *Equisetum* contains the mineral,

silica, flavonoids (isoquercetin, luteolin, and kaempferol) and the saponin, equisetin^{10, 11,13, 20, 23, 27, 28}.

Crataeva and *Equisetum* have been shown to alter urinary electrolytes in such a way so as to reduce lithogenic potentiality^{15, 16, 21}. *Crataeva* has also been found to inhibit small intestinal Na-K-ATPase¹⁴. These effects may be due primarily to the presence of the sterol lupeol. A number of studies have shown that lupeol has anti-oxaluric and anti-calcuric effects leading to increased spontaneous passing of stones and symptomatic relief^{15, 16, 28, 29}. It has been hypothesised that this passage of the stone may be produced via a tonic contractile action of the drug on the smooth muscle^{12, 15, 16}. *Equisetum* may also assist with incontinence via a similar mechanism. Kaempferol, luteolin and isoquercetin, found in *Equisetum*, are documented to inhibit xanthine oxidase and subsequent urate calculi formation²⁴.

These herbal drugs may also work through an improvement in the tone of the bladder wall. In 1982, Deshpande *et al.* reported that *Crataeva* has beneficial effects on neurogenic bladder and post-prostatectomy atony of the bladder¹². *Crataeva* administration also produced a marked relief of symptoms of frequency, incontinence, pain and retention of urine in men with hypotonic bladder as a result of benign prostatic hypertrophy. The authors concluded that *Crataeva* acts to increase the tone of the bladder and the expulsive force of urine, thereby helping effective evacuation¹². Cystometric studies analysed in this paper also demonstrate that *Crataeva* normalises the tone of the urinary bladder and significantly decreases residual urine volume.

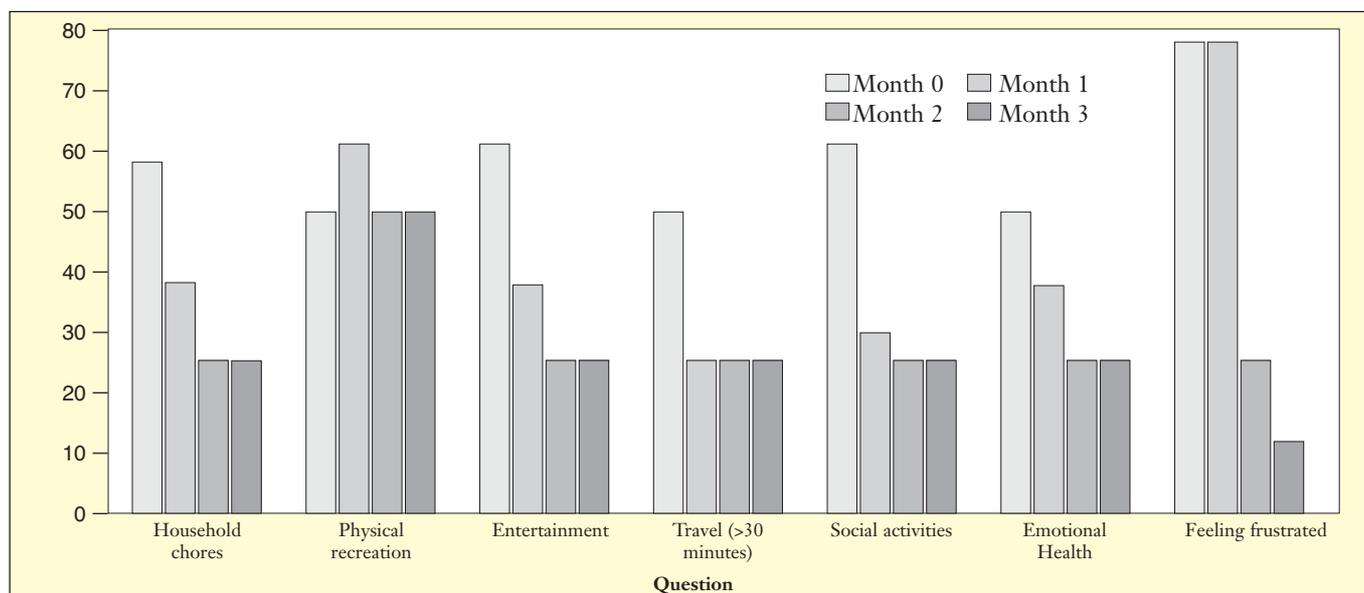
These results are also supported by animal studies where *Crataeva* has been shown to increase the tone of both smooth and skeletal muscle *in vitro*³⁰. Animal studies indicate that 40 days of treatment with *Crataeva* resulted in hypertonic curves of the urinary bladder when compared to initial curves³⁰.

Table 2. Incontinence Impact Questionnaire.

Has urine leakage affected the following:	Month		
	1	2	3
• Household chores	0.100	0.100	0.100
• Physical recreation	0.299	0.302	0.229
• Entertainment activities	0.175	0.040	0.017
• Travel greater than 30 min from home	0.040	0.052	0.052
• Social activities	0.086	0.017	0.040
• Emotional health	0.070	0.040	0.025
• Feeling frustrated	0.017	0.019	0.007

Paired T-Test p<0.05

Figure 2. Percentage of “bothered” (1, 2 or 3) responses.



It has been demonstrated in rat studies that some species of the Equisetum family have a diuretic action, indicated by the excretion of sodium, potassium and chloride similar to that of other drugs such as hydrochlorothiazide²². A more recent study using rats also demonstrated beneficial effects of the drugs in urolithiasis²¹. These authors suggest that this result could be due to the antibacterial action of the constituents, namely, the saponins.

Interestingly, *Crataeva* has anti-inflammatory and antibacterial properties^{10, 13, 17, 18, 31, 32}. Lupeol, found in *Crataeva*, has even been shown to be nephro-protective in rats exposed to toxic doses of cadmium³³. Isoquercetin, found in *Equisetum*, is known to have anti-inflammatory effects via inhibition of inflammatory prostaglandins, although *Crataeva* is thought to produce anti-inflammatory effects via a different mechanism^{23, 31}. The positive effect on chronic urinary tract infections is most likely a combination of anti-bacterial and anti-inflammatory actions.

Based upon previous clinical research, the positive results observed in this study after administration of the herbal preparation are likely to be a result of a tonic effect on the muscles of the pelvic floor, an increased ability for the urinary bladder to completely empty and decreased residual urine volume or improved tone of the urinary bladder.

While larger placebo controlled studies are now required, these results have highlighted a role for these herbal drugs in the management of urinary incontinence.

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REFERENCES

- Doran CM, Chiarelli P & Cockburn J. Economic costs of urinary incontinence in community-dwelling Australian women. *Medical Journal of Australia* 2001; 174:456-458.
- Sullivan J & Abrams P. Pharmacological management of incontinence. *European Urology* 1999; 36(1):89-95.
- Andersson KE. Drug therapy for urinary incontinence. *Baillieres Best Practice in Research Clinic Obstetrics and Gynaecology* 2000; 14(2):291-313.
- Owens RG & Karram MM. Comparative tolerability of drug therapies used to treat incontinence and enuresis. *Drug Safety* 1998; 19(2):123-39.
- Wada Y, Yoshida M, Kitani K *et al.* Comparison of the effects of various anticholinergic drugs on the human isolated urinary bladder. *Archives of the International Pharmacodynamic Therapy* 1995; 330(1):76-89.
- Steels E, Seipel T & Rao A. Herbal essential oils for urinary incontinence. *Australian Continence Journal* 2001; 7(2):34-37.
- Karantanis E, Lynch W, Louey M, Anderson P, O'Sullivan R & Moore KH. Electro acupuncture for refractory idiopathic detrusor instability or sensory urgency. *Australian Continence Journal* 2000; 6(4):6-7.
- Arya LA, Myers DL & Jackson ND. Dietary caffeine intake and the risk for detrusor instability: a case-control study. *Obstetrics and Gynaecology* 2000; 96(1):85-89.
- Bryant C, Dowell C & Fairbrother F. A randomised trial of the effects of caffeine upon frequency, urgency and urge incontinence. *Australian Continence Journal* 2000; 6(4):8.
- Nadkarni KM. *Indian Materia Medica*. Volume 1. Bombay Popular Prakashan.
- British Herbal Pharmacopeia. British Herbal Medicine Association, West Youks, UK, 1983.
- Deshpande PJ, Sahu M & Pradeep K. *Crataeva nurvala* Hook and Forst (Varuna) – the Ayurvedic drug of choice in urinary disorders. *Indian Journal of Medical Research* 1982; 76:46-53.
- Bone K. *Clinical Applications of Ayurvedic and Chinese Herbs*. Monographs for the Western Herbal Practitioner. Phytotherapy Press, Warwick, Qld, Australia 1997.
- Varalakshmi P, Latha E, Shamila Y & Jayanthi S. Effect of *Crataeva nurvala* on the biochemistry of the small intestinal tract and stone-forming rats. *Journal of Ethnopharmacology* 1991; 31:67-73.
- Varalakshmi P, Shamila Y & Latha E. Effect of *Crataeva nurvala* in experimental urolithiasis. *Journal of Ethnopharmacology* 1990; 28:313-321.
- Anand R, Patnaik GK, Kamal R & Bhaduri AP. Antioxaluric and anticalciuric activity of lupeol derivatives. *Indian Journal of Pharmacology* 1995; 27:265-268.
- Salvat A, Antonnacci L, Fortunato RH, Suarez EY & Godoy HM. Screening of some plants from Northern Argentina for their antimicrobial activity. *Letters of Applied Microbiology* 2001; 32(5):293-297.
- Xu HX & Lee SF. Activity of plant flavonoids against antibiotic-resistant bacteria. *Phytotherapy Research* 2001; 15(1):39-43.
- Schwartz BF, Bruce J, Leslie S & Stoller ML. Rethinking the role of urinary magnesium in calcium urolithiasis. *Journal of Endourology* 2001; 15(3):233-235.
- The German Commission E Monographs 1998.
- Grases F, Melero G, Costa-Bauza A, Prieto R & March JG. Urolithiasis and phytotherapy. *International Journal of Urology and Nephrology* 1994; 26(5):507-511.
- Perez Gutierrez RM, Laguna GY & Walkowski A. Diuretic activity of Mexican equisetum. *Journal of Ethnopharmacology* 1985; 14(2-3):269-272.
- D'Agostino M, Dini A, Pizza C, Senatore F & Aquino R. Sterols from *Equisetum arvense*. *Boll Soc Ital Biol Sper* 1984; 60(12):2241-2245.
- Nagao A, Seki M & Kobayashi H. Inhibition of xanthine oxidase by flavonoids. *Bioscience, Biotechnology & Biochemistry* 1999; 63(10):1787-1790.
- Robinson D, Pearce KF, Preisser JS, Dugan E, Suggs PK & Cohen SJ. Relationship between patient reports of urinary incontinence symptoms and quality of life measures. *Obstetrics and Gynaecology* 1998; 91(2):224-228.
- Tapp AJS, Cardozo LD, Versi E & Cooper D. The treatment of detrusor instability in postmenopausal women with oxybutinin chloride: a double blind placebo controlled study. *British Journal of Obstetrics and Gynaecology* 1990; 97:521-526.
- Pengelly A. *The Constituents of Medicinal Plants: An Introduction to the Chemistry and Therapeutics of Herbal Medicine*. Sunflower Herbal (2nd ed), Merriwa, NSW, Australia, 1996.
- Lakshmi V & Chauhan JS. A new pentacyclic triterpene from the root bark of *Crataeva nurvala*. *Planta Medica* 1977; 32:214-216.
- Malini MM, Baskar R & Varalakshmi P. Effect of lupeol, a pentacyclic triterpene, on urinary enzymes in hyperoxaluric rats. *Japanese Journal of Medical Science & Biology* 1995; 48(5-6):211-220.
- Das PK, Rathor RS, Lal R, Tripathi RM, Ram AK & Biswas M. Anti-inflammatory and anti-arthritis activity of Varuna. *Indian Journal of Medical Research* 1974; 9:49-56.
- Geetha T & Varalakshmi P. Anticomplement activity of triterpenes from *Crataeva nurvala* stem bark in adjuvant arthritis in rats. *General Pharmacology* 1999; 32(4):495-497.
- Geetha T & Varalakshmi P. Anti-inflammatory activity of lupeol and lupeol linoleate in rats. *Journal of Ethnopharmacology* 2001; 76(1):77-80.
- Nagaraj M, Sunitha S & Varalakshmi P. Effect of lupeol, a pentacyclic triterpene, on the lipid peroxidation and antioxidant status in rat kidney after chronic cadmium exposure. *Journal of Applied Toxicology* 2000; 20(5):413-417.