



SEIPELGROUP

FORMULATING INNOVATION

**Why Bladder Health is Key to
Healthy Aging for Millions**

My Background

Dr. Tracey Seipel, N.D.

Naturopathic Doctor, Medical Herbalist, Clinical Nutritionist, Diabetes Educator and Founder of Seipel Group, Australia.

- 30 years of experience in clinical practice
- Leader in education for Australian Naturopathic Colleges, as an advisor to government boards, developed nutritional training for Australia Medical Schools
- Formulator for many Australian and USA nutraceutical companies
- Developed the first natural Bladder formula late 1990's (urinary incontinence in women, and, then overactive bladder and incontinence in both men and women)
- Australian Medical school nutrition program
- Pioneered the bladder natural health category in the late 1990's in Australia and USA.



Bladder Problems and Their Impact

IMPACT of the BLADDER in AGING

Top 3 conditions to most adversely affect Quality of life as we age:

- Urinary incontinence
- Alzheimers and dementia
- Stroke

Urinary incontinence is a leading reason for elderly admittance to nursing care.

The Conditions

Urinary Incontinence (UI)

- Urgency UI
- Stress UI
- Mixed UI

Overactive Bladder (OAB)

- Urinary urgency
- Urinary frequency & Nocturia
- Urgency urinary incontinence

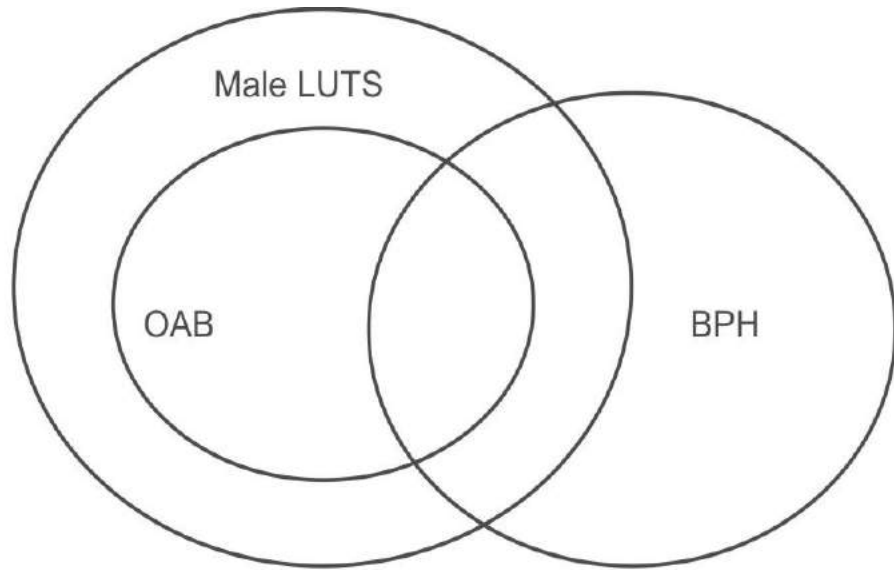
Urinary Tract Infection (UTI)

- Chronic UTI
- Interstitial (non-infective) cystitis
- Bladder oversensitivity

Male Urinary Care

- BPH
- OAB

Male LUTS: Prostate or Bladder?



Association between male LUTS, OAB and BPH



OAB

The current male urinary market focuses only on the prostate, particularly BPH.

This is only half the story.

Almost 50% of the time male urinary symptoms are due to storage problems, commonly OAB.

* Source: Chun-Hou Lia and Hann-Chorng Kuo. 2010. Incontinent Pelvic Floor Dysfunction

OAB US Statistics

Is more common than diabetes or asthma:

- Affects **37 million Americans**
- Nearly 1 in 6 suffer

(Ref: Stewart et al. Prevalence and burden of overactive bladder in the United States. *World Journal of Urology*. 2003;20(6):327–36.)

Societal costs of OAB;

- USD \$12 billion (2000 values)

(Ref: Giovanni Aguzzi, B. S. Systematic Review. *The Open Pharmacoeconomics & Health Economics Journal*, 2010.)

Overactive Bladder

- **579.6 million global cases of OAB in 2016 among adults aged 20 years and older with forecasts increasing to 649.4 million by 2025**
- **Growth of this market is driven by the increasing geriatric population and rising prevalence of bladder overactivity**
- **Cost of OAB was \$65.9 billion USD in 2007 with costs expected to increase 25% by 2020**

Ref: https://www.researchandmarkets.com/research/cdkrnp/global_overactive?w=5

Ref: Kyu Shik Kim, H. S. (2016). Antimuscarinic Agent Treatment Affecting Patient-Reported Outcomes in Overactive Bladder Syndrome With Depressive Symptoms. *International Neurourology Journal*, 350-355.

Summary of Urinary Incontinence Prevalence - NIH 2012 (Urologic Diseases in America)

Prevalence of UI in USA	Number of People
Female Stress UI	41,441,531
Female Non-stress UI	9,428,239
Male Stress UI	4,096,666
Male Non-stress UI	3,654,917
Total	58,621,353

National Institutes of Health 2012 Report

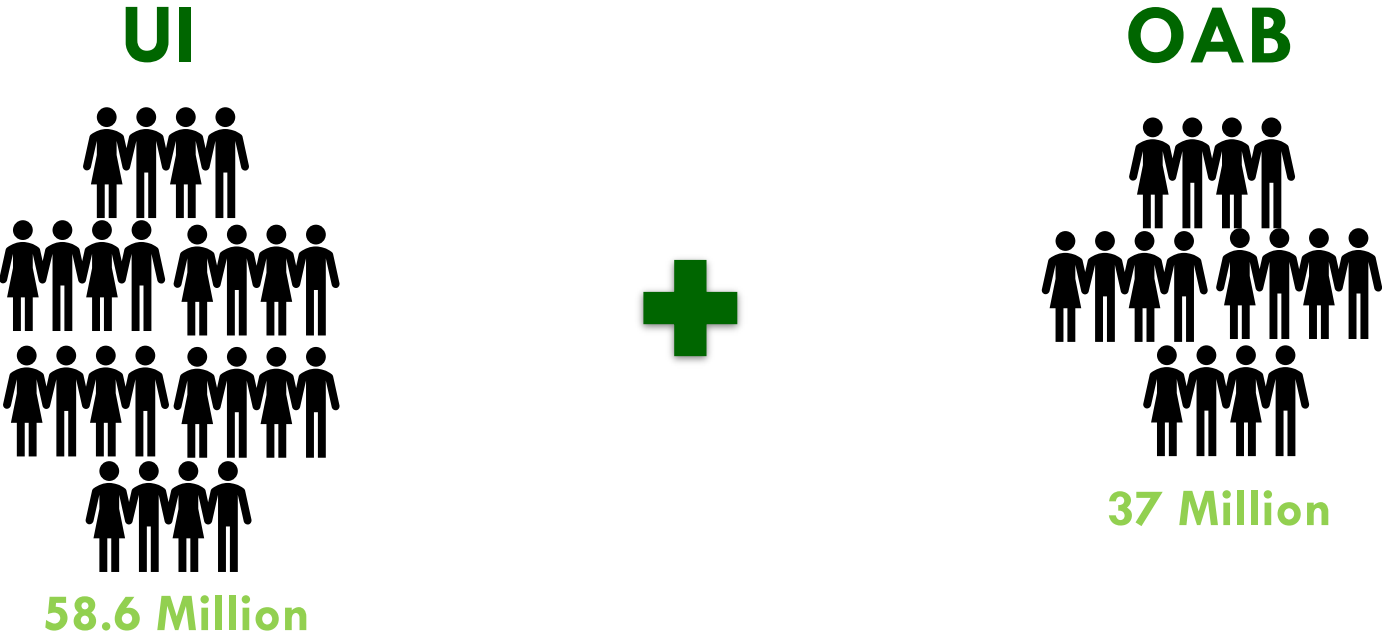
100 | Urologic Diseases In America

Table 4-2. Prevalence of stress urinary incontinence among adult females 2001-2008 (merged), count, percent^f

	Total Count	Difficulty Controlling Bladder					
		Yes		No		Refused to Answer or Don't Know	
		Count	Percent	Count	Percent	Count	Percent
Total	99,142,845	41,441,531	41.80%	57,530,091	58.03%	†	†
Age							
18-24	6,044,968	1,296,109	21.44%	4,748,859	78.56%	†	†
25-34	15,442,667	4,338,795	28.10%	11,052,844	71.57%	†	†
35-44	20,295,974	8,132,933	40.07%	12,163,040	59.93%	†	†
45-54	22,714,794	10,682,105	47.03%	12,027,586	52.95%	†	†
55-64	13,734,065	6,716,912	48.91%	7,004,106	51.00%	†	†
65-74	10,948,331	5,582,235	50.99%	5,326,928	48.66%	†	†
75-84	8,354,221	3,957,845	47.38%	4,360,507	52.20%	†	†
85+	1,607,826	734,598	45.69%	846,220	52.63%	†	†

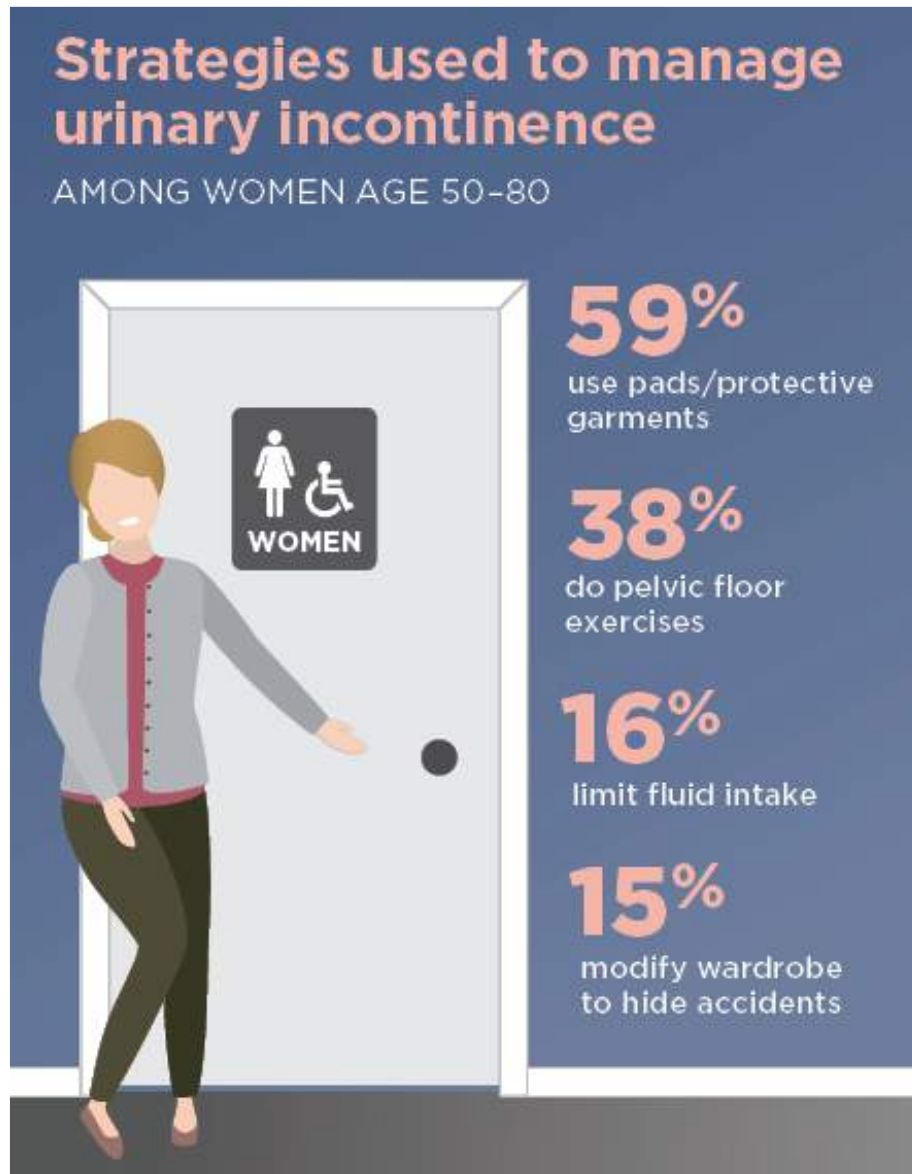
Ref: Table 4-2. Litwin MS, Saigal CS, editors. *Urologic Diseases in America*. US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. Washington, DC: US Government Printing Office, 2012; NIH Publication No. 12-7865, p100.

UI and OAB affect as many people as arthritis



UI + OAB Conservative US Estimate: >70 Million

University Of Michigan 2018 National Poll



43% of 50- to 64-year-old women reported urinary incontinence in the past year; 51% percent of 65 and older

59% of women 50-80 with UI use pads or protective garments

41% said it is a “major problem ”or “somewhat of a problem”; 1/3 had leakage episodes almost daily; nearly half said they worried about the condition worsening

79% reported leakage when coughing and sneezing; 64% reported not having enough time to reach the bathroom

40% feel embarrassed and 32% worry about incontinence odor

2/3 of patients are reluctant to bring up their incontinence to a doctor because they are embarrassed or think it can’t be helped

The important thing to realize is incontinence can be treated

Source: National poll was conducted by the University of Michigan Institute for Healthcare Policy and Innovation and sponsored by the AARP and Michigan Medicine.



The prevalence of postpartum urinary incontinence is high



Thomason AD, Miller JM, Delancey JO *International Urogynecology Journal Pelvic Floor Dysfunction*. 2007;18(2):147–151.

Lin, Y., Chang, S., Hsieh, W., Chang, Y., Chueh, H., Chao, A., & Liang, C. (2018). *Taiwanese Journal of Obstetrics & gynaecology*, 57 3, 340-345

Fritel X, Fauconnier A, Levet C, Bénifla JL. *Acta Obstet Gynecol Scand*. 2004;83(10):941–945..doi:10.1111/j.0001-6349.2004.00457.x

Hilde, G., Bø, K. (2015). *Current Women's Health Reviews*, 11, 19-30

Stress UI Postpartum

- Postpartum incontinence is reported in up to 75% of women, with pooled prevalence at 33%
- Longitudinal studies within the first year postpartum show reductions in prevalence over time, however, one study found 29% SUI four years after the first delivery
- Stress UI increases with multiple pregnancies; in a study at 1-year postpartum, SUI for first time birth (primiparous) was 10% vs. up to 30% for multiple births (multiparous)

Google Ad Word Searches (monthly):

Kegel Exercises

- Up to 1 million searches per month

Pelvic Floor Exercises

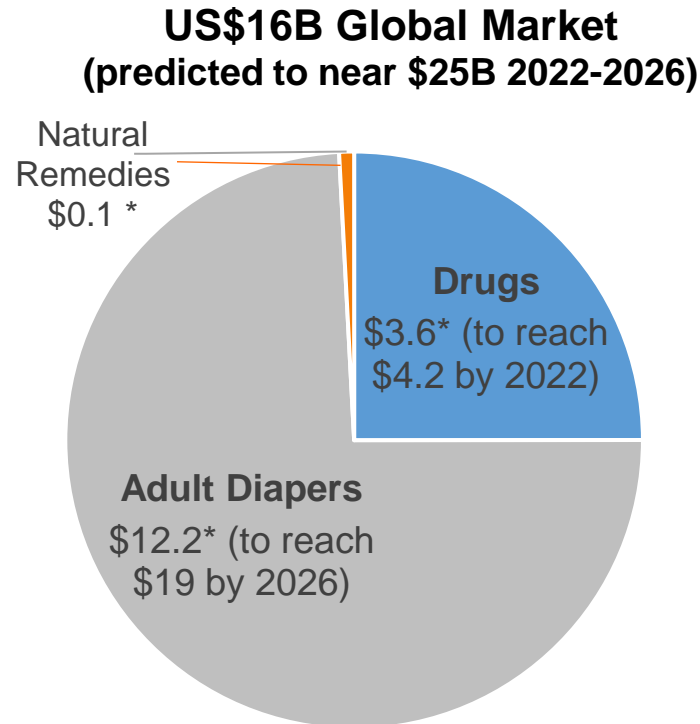
- Up to 100,000 searches per month



Pharmaceutical advertising for UI and OAB

- Increase market awareness

Urinary incontinence management is dominated by adult diapers/pads



Ref: PR Newswire, Feb 2019

<https://www.prnewswire.com/news-releases/global-adult-diaper-market-to-2023-300686415.html>; <https://www.prnewswire.com/news-releases/global-overactive-bladder-treatment-market-to-reach-usd-419-billion-by-2022---driven-by-the-development-of-new-therapies-to-treat-bladder-overactivity-300499179.html>

The Market:

Adult Diapers

- Adult diaper sales exceeding infant diaper sales - Japan
- Fastest-growing household products business
- 48% growth 2015 – 2020

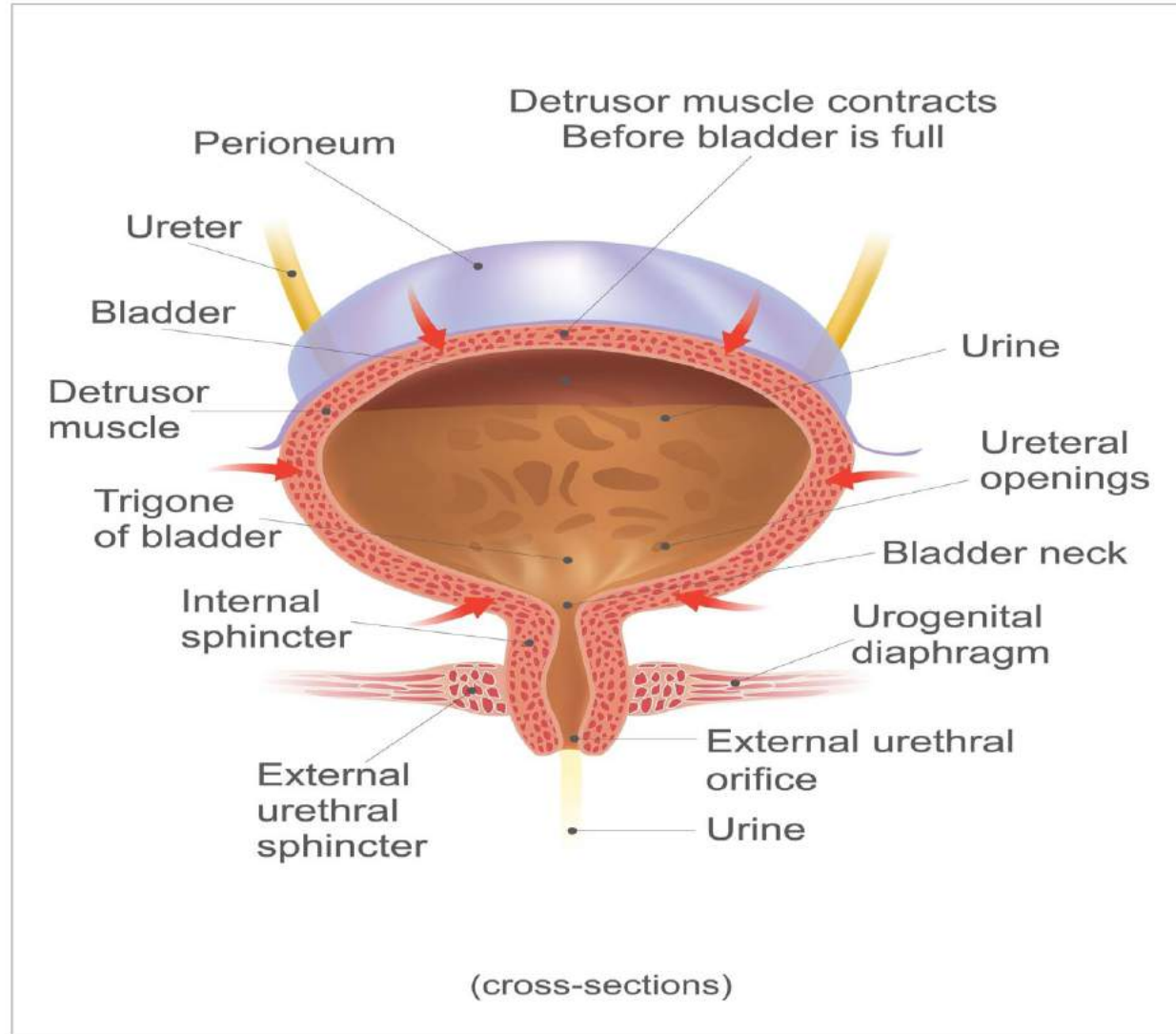
Increased Awareness

- Social stigma prevented treatment for 70% of sufferers
- Increasing acceptance of the condition driving growth
- Aging population are demanding better freedoms and health

Supplement Aisles need a Urinary Control Category

The Bladder

(Women)



Urinary Incontinence and OAB Published Placebo-Controlled Research

Herbal Comparison

Few herbals have been assessed for effectiveness in reducing urinary incontinence and OAB. Urox® was the only herbal formula to show statistically significant reductions when compared with placebo. This resulted in 3 patent families across 20 countries including USA and Canada with strong claims



PRODUCT	No. People recruited	No. People Completed	Sex	Trial Duration (wks)	SYMPTOMS &	RESULTS	(% reduction)		
					Frequency	Normal frequency achieved (# wks)	Nocturia	Urgency	Incontinence
Urox®	150	142	M & F	8	33%*	8	46%*	60%*	56% (UI)* to 67% (SI)*
Soya and Pumpkin seed	120	83	F	12	27%**	12	31%**	31%**	X
Angelica archangelica	69	66	M	8	#	#	X	#	#

*p<0.001

Not assessed

X Not statistically significant

** Comparison was not made with placebo, only with active baseline due to no statistical significance when compared to placebo

Research has been the foundation of the 20-year evolution of Urox®.

A US randomized controlled trial in the mid 2000's, ongoing standardizations and refinements followed by a second pilot trial and then comparative trial, led to today's Urox® formula:

- **1999** First formulation launched in Australia
- **2002** Steels et al, ACJ 2002. Pilot, Crateva and horsetail to improve bladder control
- **2004** Formulation changes to improve effectiveness.
- **2006** Schauss et al, FASEB. RDBPCT, 120 participants, shows Crateva and horsetail combination, UroLogic improves symptoms of urinary frequency, incontinence, urgency and nocturia in men and women.
- **2007 Steels et al. 12-month Case-controlled. Crateva and Horsetail reduces frequency, duration and severity of UTIs in women.**
- **2010** Formulation modified to produce faster effects (within 1 month versus 3) with lower dosage (reduced to 2 capsules daily, previously 4/day)
- **2011** Seipel et al, unpublished pilot trials. Urox reduces symptoms of overactive bladder and urinary incontinence.
- **2012** Seipel et al, unpublished trials. Urox with added Linderera aggregata produces faster results and within a shorter timeframe than Crateva and horsetail alone.
- **2018** Schoendorfer et al, Urox RDBPCT, 150 participants. Urox reduced day frequency, nocturia, urgency and urge and stress incontinence in men and women. Results occurred within 2 to 4 weeks. *Published BMC CAM; January 31, 2018.*
- **2021** Schloss et al, Urox RDBPCT, 48 children (6 to 14 years). Urox reduces frequency of bedwetting, urinary incontinence and urgency.

AGES of THE BLADDER Impact on Quality of Life

Aging bladder leads to:

Reduced exercise, socialising, travel

Night-time falls

Embarrassment, Loss of dignity

Reliance on diapers/padded underwear

Early admittance to nursing care



Uro[®] Published Clinical Study Results:

Produced the following improvements over 2-months:

- ✓ 60% reduction in occasional urinary urgency
- ✓ 60% reduction in occasional incontinence (both stress and urge)
- ✓ Meaningful reduction (nearly half) of occasional nighttime trips to the bathroom
- ✓ 75% Urox[®] users reduced their occasional pad usage to one or less per day
- ✓ 84% Urox[®] users felt satisfied
- ✓ 23% Urox[®] users reported normal continence after 8 weeks)
- ✓ Benefits reported in 2 weeks, with greatest benefits at 8 weeks
- ✓ No significant adverse effects or known drug interactions

<https://bmccomplementalternmed.biomedcentral.com/articles/10.1186/s12906-018-2101-4>

Schoendorfer et al BMC CAM, 31 Jan, 2018

UROX[®] 840mg daily contains:

Cratevox[™] (*Crateva nurvala*, Three leaf
caper)

(stem bark)

Equisetum arvense (Horsetail)

(aerial parts)

Lindera aggregata

(root)

General Mechanisms of Action:

- Stabilizes bladder muscles
- Independently improves tone of pelvic floor muscles
- Strengthens collagen and connective tissue of bladder and pelvic floor
- Stabilizes neural stimulation of the bladder detrusor muscle (OAB)
- No drying anticholinergic/antimuscarinic effect

Safety Summary:

- Urox[®] is very well tolerated
- Toxicology testing shows Urox[®] is:
 - NOAEL (No Observed Adverse Event Level) of 3000mg/kg bw/day or 200x the recommended daily dose of Urox[®]
- Safe for children

AGES of THE BLADDER

When and how to supplement

Bedwetting child
Hx childhood UTIs
Young women with UTI/cystitis
Urinary frequency and urgency

Post partum stress UI – increases with each pregnancy

50 years +
Menopausal/Perimenopausal UI
Male LUTS attributed to OAB and/or BPH
Elderly UTI prevention/bladder oversensitivity



Bladder control is a significant and underserved area of healthy aging

The supplement industry is moving forward with urinary, beyond UTI and BPH

Now we need to get these products into the hands of consumers





SEIPELGROUP

FORMULATING INNOVATION

www.seipelgroup.com