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Women's Health & Herbal Medicine

Range of conditions can affect women, 2 conditions are discussed here:
Urinary Tract Infections (UTIs) and Salpingitis

PHYTOCHEMICAL AND PHARMACOLOGICAL COMPARISONS OF THREE HERBS INDICATED IN COMMON URINARY TRACT DISORDERS

ABSTRACT

Herbal approaches to medical problems have had a long history of traditional use in many parts of the world. Urinary tract disorders present a range of clinical features that can be effectively addressed at the symptomatic level by the use of appropriate herbs. In this respect urinary antiseptics such as *Arctostaphylos uva ursi* (bearberry) and *Barosma betulina* (buchu) provide natural alternatives to antibiotics and synthetic diuretics in a climate that increasingly embraces therapies that are in keeping with a holistic philosophy to diagnosis and treatment. Equally, their anti-inflammatory properties indicate their general use in some of the more common complaints of the renal excretory system. Additionally, *Serenoa repens* (saw palmetto) is viewed favourably in orthodox medicine as an effective anti-inflammatory in benign prostatic hyperplasia (BPH) through its action as an anti-androgen and through its oestrogenic properties. Much of the need for invasive surgery in the growing incidence of BPH can be eliminated with the use of saw palmetto extract which appears to offer a greater appeal to both patients and orthodox practitioners.

However, as with most herbal remedies in current use today, in as much as there is compelling evidence for their efficacy, medical science requires incontrovertible pharmacological data, clinical studies and toxicology reports that conform to scientific protocol. A full and accurate understanding of the active ingredients in popular effective herbs will not only benefit herbal medicine practitioners by providing scientific credibility to the therapy, but also to patients in the alleviation of the often distressing symptoms of urinary tract disorders. In this respect, science and herbal medicine share a common purpose that will serve in the best interest of medicine in addressing treatment strategies for all human illnesses and diseases.

INTRODUCTION

Definition and Classification of Urinary Tract Disorders

The urinary tract consists of the kidneys, the ureters, the bladder and the urethra. Therefore, in essence, urinary tract disorders will involve any one of these structures and the range of symptoms witnessed in the clinical setting can be broadly based on the following categories that dictate their physiological manifestations. Conditions which are classified under urinary tract disorders have been summarised in Table 1 (Adapted from Tortora & Anagnostakos, 1990 and Haslett et al., 1999).

The renal excretory system serves a crucial function in the elimination of toxins and metabolic wastes from the body Optimum function of the system can be significantly compromised due to disorders either at the kidney level, bladder level or at the anatomical connections between the two organs (ureters). Similarly, problems could occur with the urethra; the structural tube that connects the bladder to the outside of the body. In short, disorders of the urinary tract presents a complicated clinical picture that may warrant either immediate medical assistance, orthodox medication (eg. A course of antibiotics) or equally, effective management with herbal alternatives. Regardless of the therapeutic approach, it is imperative to initially address the symptoms (without which complications could arise) but also to view the underlying mechanisms and risk factors to prevent reoccurrence at any level. (Ballinger & Patchett, 2000).

TABLE 1 : Broad Descriptions of Common Urinary Tract Disorders*(Adapted from Tortora & Anagnostakos, 1990 and Haslett et al., 1999)*

Disorder	Description
Cystitis	Inflammation of the urinary bladder caused by infection. There is undue frequency of urination, burning or 'scalding' pain on passing urine, and sometimes incontinence
Urethritis	Inflammation of the lining of the urethra usually of infective causes
Pyelonephritis	Inflammation of the pelvis of the kidney caused by bacterial infection spreading from the bladder. Chronic attacks may cause permanent damage to the kidney resulting in hypertension and kidney failure
Obstruction of the urethra (eg. Prostatitis)	Commonly due to enlargement of the prostate gland. Can be due to **prostatitis** (inflammation of the prostate gland due to a bacterial infection), **benign prostatic hypertrophy** or **BPH** (an increase in the size of the inner zone of the prostate gland) or prostate carcinoma. Prostate enlargement is characterised by urinary infrequency, hesitancy and pain on passing urine in the case of prostatitis
Renal Calculi (Kidney Stones)	Kidney stones formed as a result of crystallisation of various substances dissolved in urine (esp. during dehydration

	when urine is most conc^{d}). Stone formation is promoted by infection or abnormal amounts of crystalline substances in urine. Obstruction of the ureter by a stone results in severe pain warranting urgent medical attention
Glomerulonephritis	Acute or chronic inflammation of the glomeruli of the kidneys mainly caused by immune complexes (bacteria-antibody particles). Recovery can be complicated by persistent abnormality of kidney function
Nephrotic Syndrome	Kidney disorder characterised by the presence of protein in the urine resulting in oedema. It may follow kidney damage from glomerulonephritis or by hypertension poisoning or adverse drug reaction
Kidney Failure	Progressive kidney disease resulting in loss of function of **both** kidneys. Incapacity to excrete body wastes sufficient enough to prevent their accumulation in blood. Inevitably fatal unless dialysis or kidney transplant is carried out
Congenital Abnormalities	Kidney disorders present at birth
Kidney Tumours	Cancers of the kidney leading to renal impairment and complications that follow

Aetiological Factors in Urinary Tract Disorders

The aetiological perspectives in common urinary tract disorders are essentially two fold; those that are due to **infective** causes (UTI) and those that are due to **obstructive** causes. **Urinary Tract Infections (UTI)** are common and the range of herbal treatments used aim to address the symptomatic relief of pain and discomfort whilst tackling bacterial numbers. In this respect, a variety of urinary antiseptics prove valuable in providing safer alternatives to the current orthodox antibiotics. Herbal urinary antiseptics will be discussed in greater detail later.

Secondly, obstructive causes mainly involve the formation and lodging of stones (or **calculi**) in the urinary system. Calculi often form in fluids in which high concentrations of chemical substances are dissolved that is further encouraged and exacerbated by infection. Obstruction to urine outflow in any part of the urinary system, particularly in structures with a narrow aperture or whatever the cause of pressure build up, can result in excruciating pain that warrants immediate and urgent medical treatment. Unfortunately, it is often when any symptoms (such as pain or urinary retention/infrequency) first appear that assistance is sought, by which stage surgical intervention may prove necessary prior to herbal treatments being considered.

Similarly however, obstruction can be a secondary feature of another primary condition; notably an enlargement of the prostate gland in men. The prostate gland is susceptible to infection, enlargement and benign or malignant tumours. Due to the fact that the prostate surrounds the urethra (xref. Fig.1), any of these disorders can obstruct the flow of urine. Prolonged obstruction may result in serious changes in the urinary bladder, ureters and kidneys, and may perpetuate urinary tract infections.

Impairment of renal function could have long-term systemic implications leading to a variety of medical complications.

Benign prostatic hyperplasia (**BPH**) should be distinguished from **prostatitis**; an inflammation of the prostate gland which is invariably caused by bacterial infection. BPH however is characterised by an increase in the size of the **inner zone** of the prostate gland and though common in men over 50 years of age, the **exact** aetiology remains uncertain. In some cases, BPH can develop into **prostate carcinoma** (prostate cancer) which is clinically more significant owing to the severity of the condition and the complications associated with it. Indications of urinary tract disorder would have followed up with routine diagnostic testing that would eliminate all other possibilities prior to the confirmation of cancer.

Diagnosis of Urinary Tract Disorders

Apart from the obvious pain (**renal colic**) and general discomfort that usually accompany most urinary tract disorders, other notable signs and symptoms can range from the presence of blood in the urine (**haematuria**) to irregularities in urine outflow (such as retention, incontinence, hesitancy or infrequency). Experience of nausea and vomiting is usually an indication of pain which may radiate; **referred pain** often manifests as a constant pain in the lower abdomen, lower back, pelvis (hip) or upper thighs (Haslett et al., 1999).

In the absence of such clinical features, a **urinalysis** with specific reference to urinary tract disorders would confirm the presence of not only significant (or abnormal) **numbers** of bacteria but also the presence of **pathogenic microbes** in particular, ***Escherichia coli*** indicating an infective cause. Equally however, similar diagnostic testing for obstructive causes such as renal calculi could be indicated by the presence of significant quantities of **crystals**, usually mineral fragments of **calcium oxalate** or **calcium phosphate**, suggesting a susceptibility to kidney stones. Early warnings of BPH, prostatitis or prostate cancer is usually conducted by a rectal examination though **ultrasound**, **blood tests** and **needle biopsy** would confirm this. Invariably however, even in its early stages, prostate enlargement produces obvious clinical features (such as weak or interrupted urine flow with an increased frequency at night) that diagnostic testing by invasive techniques usually serves to confirm initial suspicions.

Herbal Therapeutic Management in Urinary Tract Disorders

Herbal therapeutic approaches in the treatment of urinary tract disorders aim to combat infection in the local area (as in urinary antiseptics) or reducing and eliminating any obstruction to urine outflow. The pharmacological strategy of **herbal diuretics** (more accurately designated **aquaretics**; Robbers & Tyler, 1999), increase the volume of urine by promoting blood flow and glomerular filtration rate (GFR) in the kidneys. They are however contraindicated in cases of oedema and hypertension due to their inability to excrete salt along with the water, but nevertheless prove useful in conditions that would benefit from an increased volume of urine. These would include minor UTI, pyelonephritis, urethriis or ureteritis or cyctitis. (Schilcher,, 1991). Similarly, increased urine flow has the added advantage of **preventing** renal calculi, by ensuring the production of a hypotonic urine (ie. more dilute than blood). A concentrated urine tends to favour supersaturation of the cystalline constituents of kidney stones and this leads to the increased susceptibility of their formation. (Coltran et al., 1994).

In patients with UTI or with stone-related and other inflammatory irritations of the urinary tract, increasing the output of a hypotonic urine appears to be an effective way to clear ascending bacteria, crystallisation nuclei and other inflammatory agents from the urinary tract, thus protecting the damaged epithelium. (Schultz et al., 1998). Though the pharmacodynamic principle with respect to the prevention of **urolithiasis** (the formation of calculi) has been challenged (Ljunghall, 1988), the principle of flushing out the urinary tract as a general treatment strategy in inflammatory urinary tract disorders remain olausible. (Schultz et al., 1998). However, whether urologic teas owe their therapeutic effect to an increased fluid intake or to the specific aquaretic actions of the administered herbs remain a source of much debate and the basis for potential research.

Table 2 lists some of the tea herbs recognised by the Commission E as having value in the treatment of inflammatory urinary tract disorders and mild renal stone disease. ((Adapted from Schultz et al., 1998).

TABLE 2 : Herbs used in urologic teas purpoted to have a diuretic action and used in treating inflammatory urinary tract conditions & mild renal stone disease *(Adapted from Schultz et al., 1998)*

Herb	Latin Name	Daily Dose (g)
Birch Leaf	*Betulae folium*	12
Dandelion Herb & Root	*Taraxaci* herba cum radice	3
Field Horsetail	*Equiseti* herba	6
Goldenrod & Early Goldenrod	*Virgaureae* herba & *Virgaureae giganteae* herba	6-12
Lovage Root	*Lavistici* radix	4-12
Nettle Leaf	*Urticae* herba	8-12
OrthosiphonLeaf	*Orthosiphonis* folium	6-12
Parsley Herb & Root	*Petroselini* herba cum radix	6
Petasite Rhizome	*Petasitidis* rhizoma	5-7
Red Sandalwood	*Santali lignum rubri*	10
Restharrow Root	*Ononidis*radix	12
Triticum Rhizome	*Graminis* rhizoma	6-9
Uva ursi Leaf	*Uvae ursi* folium	3

A number of herbs can be currently recommended according to their action for the range of urinary tract disorders witnessed in the clinical setting. For the purposes of this assignment however, **three** herbs will be discussed in detail highlighting their phytochemical and pharmacological properties that determine their specific indications. *Arctostaphylos uva ursi* (bearberry), *Barosma betulina* (buchu) and *Serenoa repens* (saw palmetto) will be profiled in detail enabling a comparison of their properties and actions that make them suitable for specific urinary tract indications.

Arctostaphylos uva ursi (Bearberry)

Arctostaphylos means bearberry in Greek, *uva ursi* means bearberry in Latin. Despite its common name, it is the dried leaves, not the berries of this widely-distributed, trailing evergreen shrub that are attributed to its medicinal properties. (Tyler et al., 1993). Its botanical profile indicates that it is a low shrub with long, creeping, densely-leaved stems with ascending branchlets. The leaves are leathery, glossy dark green on the upper surface and pale green on the underside. There are usually about 3-12 flowers with an urn-shaped corolla, white to pink in colour and stamens with purplish anthers (xref. Fig 2; taken from Stary, 1998). The fruit is a globe-shaped, dark red stone with 5 seeds inside. In favourable conditions, growth of bearberry is such that it may form a dense carpeting ground cover. If the main root is destroyed however, the whole plant dies. (Stary, 1998).

Family : Ericacea

***Atctostaphylos uva ursi* (Bearberry)**

Habitat : Temperate zones of N. Hemisphere (N. America & Europe)

PU : Dried Leaves

PR : Bitter, Astringent

AC : Arbutin (7-9% of leaves)
Tannins (6-7%)
Flavonoids (Quercitin)
Allantoin, Gallic & Ellagic Acids,
Volatile Oils & a resin (Urvone)

Summary : Antibacterial, Diuretic, Astringent,

Actions Soothing, Tonic

FIGURE : Photo picture of *Arctostaphylos uva ursi* depicting botanical features of the corolla and fruit with seed arrangement (Taken from Stary, 1998)

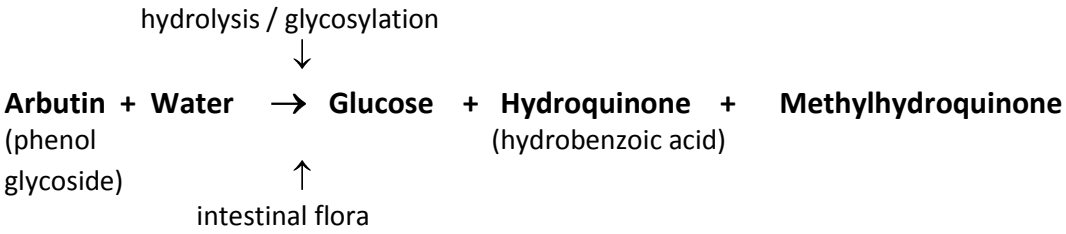
The German Commission E recommends bearberry as a treatment for inflammatory conditions of the urinary tract; it is considered to have an antiseptic action, namely bacteriostatic. However, its antiseptic property is only really effective when urine is alkaline. This is due to the fact that the leaves contain approx. 10% of the most important active princple; **arbutin**. This active chemical is split into glucose and **hydroquinone** in the kidney and it is the hydroquinone that exerts an antiseptic action on the urinary passages. (Weiss, 1994). To ensure an alkaline urine, consumption of a diet that is rich in milk, vegetables (especially tomatoes), fruits, fruit juices and potatoes will be necessary. In addition, consumption of 6-8g of sodium bicarbonate per day will assure alkalinity. (Robbers & Tyler, 1999).

History and Folk Use

Uva ursi has a long history of use for its diuretic and astringent properties. Conditions for which it was used include bladder and kidney infections, kidney stones and bronchitis. (Leung, 1980). It was also believed to impart tone to the urinary passages and to exert an antiseptic action there. (Tyler, 1993).

Phytochemistry, Pharmacokinetics and Pharmacodynamics

The quantities of the active constituents of *A. uva ursi* vary greatly according to different texts but there appear to be some parity in their actual presence. The principle, most active ingredient; **arbutin** (approx. 7-10% in leaves), is poorly absorbed from the gastrointestinal tract. Nevertheless, upon entering the body, it undergoes a chemical change that yields **hydroquinone** (and methylhydroquinone) which confers its **antibacterial** property to the herb. It is for this reason that bearberry is effective in treating inflammation of the kidneys. (Willard, 1993). The biochemical changes that occur can be summarised by the following :-



Relatively little is known about the pharmacokinetics of arbutin; all data are based on studies by Frohne (1986). The aglycone hydroquinone (unlike arbutin) is well absorbed from the gut probably via conjugation in the intestinal mucosa or liver, and excreted as a conjugate via the renal pathway (Schultz et al., 1998). Though supported only by scant experimental data, the concept of hydroquinone's antiseptic properties lies in the belief that under conditions of an alkaline urine, hydroquinone reforms from the conjugates and exert antibacterial properties when present in sufficient quantities. The skeletal structure is shared by both arbutin (R=OH) and methylarbutin ($R=OCH_3$) (Mills & Bone, 2000).

Studies using the isolated hydroquinone compound in the form of arbutin in the investigation of its antibacterial property reveal that bacteria in the gut/ intestine break down much of the arbutin before it is absorbed. If on the other hand, the whole plant is given, components in the plant prevent this breakdown. (Frohne, 1970). This enables an improved absorption of the intact arbutin conversion to hydroquinone upon administration of the whole plant or crude extract (Murray, 1995).

Much of the evidence of hydroquinone's antimicrobial action over arbutin has been generated from animal studies. It is effective against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Mycobacterium smegmatis*, *Shigella sonnei*, and *Shigella flexnevi*. (Moskalenko, 1986). Interestingly, the antimicrobial activity of arbutin towards bacteria implicated in producing UTI has been found to be directly dependent on the β-glucosidase activity of the infective organism. (Jahodar et al., 1985). Human studies show hydroquinone to exert an antiseptic and astringent action on the urinary mucous membranes. (Frohne, 1986 and Stahl, 1973). Importantly however, the the **tannins** present are of the **hydrolysable** type; gallic acid in the crude extract may prevent β-glucosidase cleavage of arbutin in the GIT before absorption, thereby increasing the amount of hydroquinone released during renal excretion. (Newall et al., 1998). Additionally, common bladder infections due to excess sugar levels in

diabetic urine can be treated effectively with *A. uva ursi*. (Green, 1991). Moreover, *A. uva ursi*'s anti-inflammatory activity was also demonstrated using rat paw oedema tests against a variety of chemical inducers such as **carrageenan**, **histamine** and **prostaglandins**. (Shipochliev & Fournadjiev, 1984).

Much of the current literature on *A. uva ursi* comment on its diuretic action on the kidneys. Weiss (1994) contradicts this, claiming that it has no diuretic action (though it is generally assumed). He suggests that it is pointless to administer large quantities of the tea in order to flush the urinary passages since it will only serve to **aggravate** and **irritate** the tissues of the bladder especially in **inflammatory conditions** such as acute cystitis. He advises its use as an **essential** measure in **chronic catarrh** conditions of the urinary tract (ie. where there is congestion and discharge), where it is both indicated and effective. For a diuretic effect, Weiss (1994) suggests the usual herbal diuretics such as dandelion rather than bearberry leaves.

Other Actions of Bearberry

According to the source, there are marked differences in the tannin content of bearberry; an important constituent that confers additional properties to this herb. Quantities in the leaves can vary (quite widely in some instances) from 10-20% (Schultz et al., 1998), 6-8% (Murray, 1995) to 15-20% (Tyler, 1993). Perhaps such variances could be due to differing habitats and cultivation methods. Nevertheless, relatively high concentrations of tannins ensure the astringent property of this herb. In this respect, bearberry renders itself effective in chronic inflammatory conditions of the urinary tract such as **cystitis** or **urethritis** though its use is limited to about **2-3 weeks** due to the high **tannin** content present in the leaves. (Schultz et al., 1998). The tannins are believed to cause stomach upset in some (Tyler, 1993), but Weiss (1994) recommends adding **peppermint** leaves to the preparation in equal parts as a prophylactic measure. Table 3 highlights other notable components in bearberry leaves (Adapted from Newall et al., 1998).

TABLE 3 : Phytochemical constituents of *Arctostaphylos uva ursi* (fol).
(Adapted from Newall et al., 1998)

Constituent	Comment
• Flavonoids	Flavonols (eg. myricetin, quercitin) and their glycosides incl. Hyperin, isoquercitin, myricitrin and quercitin
• Iridoids	Asperuloside (disputed), monotropein
• Quinones	Total content at least 6%, mainly arbutin (5-15%) and methylarbutin (glycosides) with lesser amounts of piceoside (glycoside), free hydroquinone and free *p*-methoxyphenol
• Tannins	6-7% (range 6-40%). Hydrolysable-type (eg. corilagin pyranoside) : ellagic and gallic acids (usually associated with hydrolysble tannins)
• Terpenoids	α-amyrin, α-amyrin acetate, β-amyrin, lupeol, uraol, ursolic acid and a mixture of mono and di-ketonic α-amyrin derivatives
• Other constituents	Acids (mallic, quinic), allantoin, resin (eg. ursone), volatile oil (trace), wax
• Other plant parts	The root is reported to contain unedoside (iridoid glycoside)

Practical Implications for Administration

Pharmacological preparations of *uva ursi* usually favour an **infusion** but this is not advisable in light of the high tannin content in the leaves that is readily extracted with hot water. For this reason a **cold maceration** is preferred in order to reduce the tannins in the preparation. Moreover, a cold maceration (1.5-4g) has the added advantage of preventing tannin-associated constipation that often occurs as a side effect of high tannin preparations. Additionally, **liquid extracts** (1:1 in 25% alcohol) may also be taken (1.5-4ml tds). Similarly 2-4ml of a **concentrated infusion** or a 15-30ml of a **fresh infusion** provide other alternatives for administration.

The impracticality and general difficulty in maintaining an **alkaline** pH (conditions in which hydroquinone exerts its antiseptic action) for an extended period of time when taking this herb, significantly impairs the usefulness of bearberry. (Robber & Tyler, 1999). As previously discussed, dietary and practical measures that ensure the alkalinity of the urine are further considerations in the administration of this herb.

Toxicity and Contraindications

Due to the high tannin content of bearberry leaves, it is **not suitable** for long-term use (Mills & Bone, 2000). Overdosing can lead to inflammation and irritation of the bladder as well as of the mucous membranes. Liver damage may be an added problem especially with children, due to possible **hepatotoxity** by the hydroquinones released. It is specifically for this reason that it is contraindicated in children under 12 years of age. (PDR for Herbal Medicines, 1998).

Side effects of bearberry infusion are uncommon though due to the high tannin content, some may report **cramping**, **nausea**, **vomiting** and **constipation**. (Mills & Bone, 2000). The serious problem lies in the toxicity of the hydroquinone which is a recognised toxic compound especially when ingested in large quantities; 1g equivalent to 6-20g of plant material has caused **tinnitus**, **nausea** and **vomiting**, **sense of suffocation**, **shortness of breath**, **cyanosis**, **convulsions, delirium** and **collapse**. A dose of 5g (equivalent to 30-100g of plant material) has proved fatal. (The Merck, 1989).

Studies into the mutagenic or carcinogenic properties of *uva ursi* leaves reveal that though arbutin is **not** mutagenic, any hydroquinone that is produced following its breakdown could exert its **mutagenic potential**. (Mueller & Kasper, 1996). Additionally, bearberry is believed to possess **oxytocic** properties (Weiss, 1994) although ***in-vitro*** studies report a **lack** of uteroactivity (Newall et al., 1998). Nevertheless, in view of the potential toxicity of hydroquinone, most literature sources advise against taking this herb during pregnancy and lactation.

Pharmaceutical Comment

Despite the alarming reports of toxicity and potential mutagenicity of hydroquinone derivatives, the documented pharmacological actions justify the use of this herb especially as an antiseptic in UTIs. Provided that sensible precautions are taken and instructions for use are followed (therapeutic doses of *uva ursi* are thought not to represent a risk to human health; Mabey, 1988), bearberry remains one of the most important herbal remedies in the natural fight against urinary tract disorders. However, it is to be accepted that clinical information is lacking and further studies are very much required in order to determine the true usefulness of *uva ursi* in infective and inflammatory conditions of the urinary tract.

Barosma betulina (Buchu)

A herb that is comparable to *uva ursi* is buchu (*Agathosma betulina or Barosma betulina*), which is used as a **urinary antiseptic** and a **diuretic** in Western Herbal Medicine. However, its traditional medicinal use in its country of origin; South Africa, also proves its worth as a stimulant and in the symptomatic relief of digestive complaints. (Chevallier, 1997). Urinary tract disorders such as acute **cystitis**, **urethritis**, **prostatitis** or **irritable bladder** are effectively treated with buchu often in combination with other herbs such as **cornsilk** (*Zea mays*), **juniper** (*Juniperus communis*) and *uva ursi*.

History of Use

Traditionally, buchu had a variety of medicinal uses, however, its principle use was in the treatment of chronic diseases of the genito-urinary tract including chronic inflammation of the mucous membranes of the bladder, irritable conditions of the urethra, in urinary discharges (particularly mucus or mucopurulent discharges), abnormally acidic urine with a constant desire to urinate with little relief from micturition, and incontinence associated with a diseased prostate. (Felter & Lloyd, 1983).

***Barosma betulina* (Buchu)**

Family :	Rutaceae
Habitat :	Hot, sunny climates in well-Drained soils
PU :	Dried Leaves
Properties :	Strongly aromatic taste, Peppermint-like odour
Main AC :	Volatile oil (1-3%), Flavonoids,
Key Actions :	Urinary antiseptic, Diuretic
Indications :	UTI, dysuria, cystitis, urethritis & prostatitis

(Bown, 1995 and Mills & Bone, 2000)

FIGURE : Picture of *Barosma betulina* (buchu). (Taken from McHoy & Westland, 2000)

There is very little scientific study that has been carried out on this herb to validate its therapeutic utility in the treatment of urinary tract disorders. Its reputed diuretic and anti-inflammatory activities are probably attributable to the **irritant** nature of the **volatile oil** and **flavonoid** components respectively. (Newall et al., 1998). Table 4 highlights the main chemical constituents of buchu. (Adapted from Willard, 1993 and Newall et al., 1998).

TABLE 4 : Key constituents of *Barosma betulina* (buchu)
(Adapted from Willard, 1993 and Newall et al., 1998)

Constituent	Comment
• Flavonoids	Diosmetin, quercitin, diosmin, quercitin-3,7-diglucoside
• Volatile Oils (1-3.5%)	Over 100 identified compounds incl. Diosphenol, limonene, menthone and pulegone as the major components
• Sulphur Compounds	-
• Mucilage	-
• Coumarins	-
• Resin	-

Note. *Other species such as Agathosma crenulata are not suitable for medical use due to their lower diosphenol content and higher pulegone content in their essential oil.(Kaiser et al., 1975).*

Buchu can be administered as an infusion (1-2g dried leaf tds), 0.3-1.2ml of liquid extract (1:1in 90%) or 2-4ml of tincture (1:5 in 60%). (Bradley, 1992 and British Herbal Pharmacopoeia, 1990).

There are contradictory reports on the safety and prolonged use of buchu. Whereas some sources suggest that this herb can be taken over an extended time period; there is no scientific data available of its toxicity (Mills & Bone, 2000), other sources warn of the **potential** toxicity of its volatile oil component (Maber, 1988). Excessive doses are not advised and it should be **avoided** in kidney infections as well as administration on an empty stomach. Occasionally, gastrointestinal intolerance and stomach irritation may occur as a side effect (regardless of duration of use) and is a safety consideration for those who have GIT problems or sensitivity. (Mills & Bone, 2000).

There appears to be more parity on information relating to the use of buchu in pregnancy and lactation. As with most herbal remedies, buchu is **contraindicated** in pregnancy (British HM Assoc., 1992) since its safety has not been established. Some advise against its use due the potential toxicity and irritant action of the volatile oil. (Newall et al., 1998).

Herbal Pharmacology

Despite its strong traditional use and modern application in urinary tract disorders, there is limited chemical data and scientific evidence on the mode of action or a substantial study of buchu that justify its medicinal uses. One possible theory suggests that its reputed diuretic and anti-inflammatory activities can be attributed to the irritant nature of the volatile oil and flavonoid components respectively (as previously stated). However, this remains speculative, but with a lack of information from credible toxicology studies, buchu may be safely used in therapeutic doses provided that guidelines and precautions are followed with a clear emphasis on the avoidance of overdosing. It is evident that research into buchu's safety and efficacy is much needed especially in light of its effective treatment in inflammatory urinary tract conditions in addition to its diuretic action on the renal excretory system.

Serenoa repens **(Saw palmetto)**

An indirect cause of urinary problems in men is an enlarged prostate gland. Enlargement may occur as a result of inflammation (**prostatitis**) or abnormal cellular tissue growth with age (**BPH** or **prostate carcinoma**).

Orthodox treatment for prostate enlargement can be drug-based for eg. **anti-androgens** such as finestride (marketed as ***Proscar®*)** or the utilisation of invasive techniques usually as a measure in chronic cases where the condition is unresponsive to medication. Surgical intervention includes **transurethral prostatectomy (TURP)** in which a resectoscope is passed into the urethra and the obstructive tissue is removed by cutting. Any bleeding is **cauterised** (heat-sealed) with an electrode. Another procedure involves **retropubic prostatectomy** where the prostate gland is removed via an abdominal incision. As is to be expected, there are many complications as a result of such procedures and not surprisingly, non-invasive measures that can reduce and prevent further enlargement of the gland appears to offer a safer and popular alternative.

The Popularity of Saw Palmetto

The most notable remedy from the southern USA is saw palmetto (*Serenoa repens* aka *Serenoa serrulata* or *Sabal serrulata*). Saw palmetto is one of the few herbs that seems to have a wider acceptance in the orthodox management of BPH being increasingly embraced by orthodox practitioners and where there **is** adequate **scientific** evidence to challenge the orthodox view of herbal remedies – this is indeed encouraging !

A study published in the British Journal of Clinical Pharmacology in **1984** found that saw palmetto extract (at dosages of 320mg/day) **increased** urinary flow rate by **over 50%**, **decreased** urine residue by nearly **42%** and significantly **reduced** the subjective symptoms of BPH. (Foster, 1996). Another report published in the British Journal of Pharmacology in **1993** found that saw palmetto berry was much more effective than a leading prostate drug in impacting urine flow in men with BPH. (Wellness Advocate, 1994).

Saw palmetto appears to share the **same** pharmacological mode of action as anti-androgens and has been widely used in Europe since the 1930s. In the USA, it has been found to be the **sixth** best-selling herb. (Walker & Brown, 1998).

Extracts of saw palmetto berry are being used extensively throughout the world for the relief of BPH. Both the **French** and **German** governments **approve** the lipophilic extracts for this purpose. Positive results with saw palmetto have been confirmed in numerous open as well as double-blind, placebo-controlled clinical trials. All of these studies demonstrate statistically significant **improvements** in the symptoms of BPH, which included increased volume and rate of urine flow, alleviation of pain, night time urinations and decreased numbers of voidings per day. Overall, these studies showed a **consistent benefit** of saw palmetto extract with virtually no side effects of any consequence. Recommendations of dietary measures in conjunction with this herb, in particular supplementations of **selenium** and **zinc** show remarkable improvements in symptoms. (Walker & Brown, 1998).

A striking characteristic of these studies is that most subjects experienced relief within days of beginning the therapy, with benefits continuing to improve over time in many cases, as much as one year of continuing improvement. Most studies were terminated after 30, 60 or 90 days.

Current Pharmacological Perspectives

The best known therapeutic approach is based on the most widely favoured hypothesis on the pathogenesis of BPH which proposes an increase in testosterone synthesis accompanied by an increase in the oestrogen : androgen ratio (Schultz et al., 1998). Treatment aims to **inhibit** the two prostatic **enzymes** that are responsible for the hormonal changes; notably **5α-reductase** (which converts testosterone to dihydrotestosterone; DHT) and **aromatase** (which converts testosterone to oestrogens). Changes in the binding capacity of sex-hormone-binding-globulin (**SHBG**) have also been implicated in the pathogenesis of BPH (Schmidt, 1983). Several *in vitro* studies on mice and rats not only demonstrated the **antiandrogenic actions** of saw palmetto extracts but also confirmed inhibitory effects on 5α-reductase. (Murray, 1995). Figure 7 illustrates the metabolism of testosterone (taken from Schultz et al., 1998).

Botanical Description

Saw palmetto is a small palm tree native to the West Indies and the Atlantic coast of N. America from South Carolina to Florida. Its height can range from 6 to 10 feet, characterised by large 2-4 foot high spiny-toothed leaves (rather like a saw; hence the name). These leaves form a circular, fan-shaped outline. It is the berries that are used for medicinal purposes. The deep red-brown to black berries are wrinkled, oblong and 0.5-1 inch long with a diameter of 0.5 inches. (Duke, 1985).

The metabolism of testosterone: The hormonal hypothesis for prostatic hyperplasia is based on the assumption of increases DHT synthesis in the prostate and a shift in the androgen/oestrogen ratio in favour of oestrogens. This implies that the inhibition of a α- reductase and aromatase would be of therapeutic benefit. SHBG = Sex-Hormone-Binding-Globulin (*Taken from Schultz et al., 1998)*

***Serenoa repens* (saw palmetto)**

Family : Arecaceae (Palmea)

Habitat : South Carolina to Florida*

PU : Fruit / Dried Berries

Main AC : Volatile Oils, Fatty Oils, Acids, Tannins, Sugars, Polysaccharides, possible anti -androgenic principles in Acidic Lipophilic fraction of berry (Tyler, 1994)

Key Actions : Anti-inflammatory, Endocrine Agent, Spasmolytic, Possibly Anti-androgenic (Mills & Bone, 2000)

Indications : Male reproductive tonic, Infections of Prostate & Genito-Urinary organs* ↑ tone of bladder, nourishes nervous system

FIGURE 8 : Picture of *Serenoa repens*

*****_There is some variation in information on the habitat; Weiss (1994) reports its growth in Mediterranean countries from Southern Spain and Majorca down to North Africa. Also some sources recommend that saw palmetto **not** be used in the treatment of bacterial prostatitis (Ottariano, 1999)._

Traditional Uses

Under the title 'Serenoa', saw palmetto was an 'official' drug from 1906-1950 and was once widely used for a variety of ailments, particularly those of the **urogenital** type. (Robbers & Tyler, 1999). The American Indians used saw palmetto berries in the treatment of **genitourinary tract disturbances** and as a **tonic** to provide nutritional support for the body. It was administered to men to increase the function of the testicles and relieve irritation in mucous membranes, particularly cases of inflammation of the genitourinary tract and **prostatic hypertrophy**. (Mills & Bone, 2000). It was also given to women with disorders of the mammary glands; its long-term use was reputed to cause its gradual enlargement. (Murray, 1995). Many herbalists consider it to be an aphrodisiac. (Duke, 1985 and Mills & Bone, 2000).

Though the active anti-androgenic principles of the berry remain unidentified, they are known to reside in the **acidic lipophilic fraction** of the drupes. (Tyler, 1994). Table 5 summarises the main constituents of saw palmetto extract of berries. (Adapted from Duke, 1985 and Wren, 1988).

Pharmacological Actions

Unlike some of the other herbs that are used medicinally, there is significant scientific evidence on the mode of action of saw palmetto extract. Studies have involved both ***in-vitro*** studies using rat and human tissue as well as ***in-vivo*** studies, namely, on rats. Additionally, numerous studies on humans have also been documented investigating the use of saw palmetto in BPH. Placebo-controlled, double-blind clinical studies carried out on more than 2000 BPH patients in Germany have confirmed the effectiveness of a saw palmetto extract. (Tyler, 1994).

TABLE 5 Key Chemical Constituents of Saw Palmetto Extract of Berries
(Adapted from Duke, 1985 and Wren, 1988)

Constituent	Comment
Carbohydrates (28.2%)	• Invert Sugar • Mannitol • High Mol Wt. Polysacc (eg. MW 100,000) with galactose, arabinose & uronic acid
Fixed Oils (26-7%)	• Many free fatty acids & their glycerides • Saturated Fats (Capric acid, caproic acid, caprylic acid, lauric acid, myristic acid, palmitic acid, stearic acid) • Unsaturated Fats • Oleic acid
Steroids	• β-sitosterol-3-D-glucoside
Acids	• Anthranilic acid • Caffeic acid • Chlorogenic acid

Other Constituents	• Flavonoids • Carotene (pigment) • Resin • Tannin • Volatile Oil (1.5%)

In short, saw palmetto **inhibits** the production of the enzyme **5α-reductase** and **3-ketosteroid reductase** (Carilla et al., 1984 and Sultan et al., 1984). These enzymes are responsible for the **conversion** of testosterone to the more reactive **dihydrotestosterone** (**DHT**); a probable mediator in BPH. Saw palmetto **blocks** the binding of DHT to the prostate cells and thus inhibits its enlargement (Ottariano, 1999). Though the active anti-androgenic principle remain unidentified, it has been found that several common dietary fatty acids (eg. linoleic acid) exerts a stronger inhibitory effect on 5α-reductase than equivalent concentrations of saw palmetto extract (Niederprum et al., 1994). Most synthetic anti-androgens such as the α adrenergic blockers (eg. terazozin) have been reported to inhibit DHT binding at androgen receptors, whilst others such as finestride (*Proscar*®) have been found to inhibit the action of 5α-reductase (Carilla et al., 1984). Saw palmetto extract has been reported to inhibit both these activities unlike their synthetic counterparts (Sultan et al., 1984). Figure 9 illustrates the mode of action of synthetic anti-androgens; the same sites of action proposed for saw palmetto extract. (Taken from Robbers & Tyler, 1999)

On a comparative level however, it appears that saw palmetto extract is several thousand times less potent as a 5α-reductase inhibitor than finestride since the concentration required to produce inhibition is far higher than that used in clinical therapy. (Rhodes et al., 1993). Furthermore, steroid 5α-reductase inhibition should result in a decrease in prostate size (x.ref Fig.9) but this has not been demonstrated with saw palmetto (Vahlensieck et al., 1993). This suggests a mechanism of action that involves diminishing prostatic **smooth muscle tone**. Experimental evidence reveals that the **spasmolytic** effect on smooth muscle contraction is by the **inhibition** of **Ca^{2+} influx** at the plasma membrane level and **not** the blocking of α_1-adrenergic receptors. (Gutierrez et al., 1996). Moreover, the hexane extract of saw palmetto has been shown to **inhibit** the action of 3α-ketosteroid reductase on DHT, which has also been implicated in the pathogenesis of prostatic hypertrophy in dogs. (Sultan et al., 1984). The pharmacological actions of saw palmetto are therefore thought to indicate a possible **multisite inhibition** of androgen action. (Newall et al., 1998).

Clinical Trials

Though the current balance of evidence implies that saw palmetto extract does not possess clinically significant inhibitory activity on 5α-reductase, the herb has been used in the treatment of mild to moderate BPH for hundreds of years. Modern clinical evidence on the liposterolic extract of saw palmetto strongly supports its efficacy in BPH and whilst this has not yet been disputed, it is sufficient to justify its use in circumstances where conventional therapy is not possible. (Mills & Bone, 2000). Moreover, the safety profile of herbal preparations is very good, appealing to those who are concerned about toxicity issues and potential complications, as well as to those currently on conventional, orthodox medication for other conditions that are symptomatic of age and decline.

Pharmaceutical Considerations

Compared to *A.uva ursi*, saw palmetto is relatively safe to use long-term with no serious side effects being officially recorded. This can be argued since a lack of substantial clinical data on adverse effects of administration does not necessarily translate to the endorsement of herb usage in large quantities. Nevertheless, only one withdrawal from a human study due to **gastric side effects** was reported. (Tasca et al., 1985). **Fatigue** and **depression** were additional side effects which may influence the continued use of saw palmetto extract. (Descotes et al., 1995).

Furthermore, other documented human studies show that saw palmetto appears to be **well tolerated** causing **no** haematological or biochemical changes and **no** contraindications or interactions are known at present. (Mills & Bone, 2000).

However, in view of the reported anti-androgenic and oestrogenic activites, saw palmetto may affect existing hormonal therapy, including the oral contraceptive pill and hormone replacement therapy. Lack of toxicity data and documented pharmacological actions dictate that this herb should be used with care (as with all herbs) and its use in pregnancy and lactation as well as its excessive use be avoided. (Newall et al., 1998). In short, a sensible approach that considers precautionary measures and awareness of current literature on the use of this herb (as with all herbs) is always strongly encouraged.

CONCLUSION

In summary, it can be seen that the clinical presentation of urinary tract disorders is such that the symptomatic herbal therapeutic management of such conditions discussed in this essay, provide effective alternatives to their orthodox counterparts. In this respect, *Arctostaphylos uva ursi* , *Barosma betulina* and *Serenoa repens* are proving their worth in alleviating the distressing symptoms that often accompany urinary tract disorders. However, notwithstanding their traditional uses and current applications in a range of urological conditions, there is a growing need for greater credible pharmacological data on their efficacy that conforms to scientific protocol. Issues of toxicity, herb-drug interactions, contraindications and side effects may reveal additional findings that could prove invaluable in conventional medicine. This is particularly apparent where current orthodox regimen remains limited or unsuccessful in the long-term management of disorders of the renal excretory system.

Future scientific studies of herbal remedies is largely dependent on funding and resources which remain a perennial problem in herbal medicine research. Optimistically though, in a climate of increasing acceptance of alternative health care strategies, conventional science is viewing traditional methods and remedies as potential sources of developing new drugs. Research opportunities may be present for studying herbal remedies at a biochemical and pharmacological level that enables a greater understanding and respect for the traditions that have maintained their medicinal applications. This is pertinent not only for the treatment of urinary tract disorders but also for the implications that it has in the therapeutic management of a range of other human disorders.

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SALPINGITIS

Definition

Inflammation of the fallopian tubes, usually as a result of an ascending infection that has spread from the vagina through the cervix and uterus. It is usually classified under the PIDs*, along with endometriosis amongst others. It is often associated with:-

- sexual intercourse
- transcervical surgery (D & C or evacuation)
- intrauterine foreign bodies eg. IUD
- retained products of conception
- blood-borne infection (very rare)

Salpingitis of infective causes may spread into the abdominal cavity, where it infects the peritoneum (peritonitis). Diagnosis of PID depends on 3 findings:-

- abdominal tenderness
- cervical tenderness
- ovarian, fallopian tube or uterine ligament tenderness

Additionally, diagnosis is based on at least one of the following:-

- fever
- leucocytosis (▯ ▯WBC▯)
- pelvic abscess or inflammation
- purulent cervical discharge
- presence of certain bacteria in smears

Aetiology

Most common causes appear to be of infective origin; Chlamydia, Neisseria or an infection acquired after childbirth. Damage resulting from infection is the most common cause of tubal infertility. Other organisms are implicated but there is conflicting medical opinion as to which are of the most important aetiology in salpingitis. Possible polymicrobial aetiology (more than one species involved).

Non-infective causes:-

- adjacent or distant inflammatory process eg. appendicitis, diverticulitis
- haematogenous dissemination of an infection from any source
- irritants or drugs intruding during uterine insufflation or hydrotubation
- insertion of IUD
- 'post-sterilisation syndrome'

* PID is a collective term for any extensive bacterial infection (primarily involving Chlamyidia trachomatis, Neisseria gonorrhoea, Bacteroides, Peptostreptococcus & Gardnerella vaginalis) of the pelvic organs esp. the uterus, fallopian tubes or ovaries.

Pathogenesis

Congested and oedematous fallopian tubes are infiltrated by polymorphonuclear leucocytes. The endotubal mucosa exudes seropurulent fluid and the mucosal folds may be destroyed or agglutinated (stuck together) by fibrinous adhesions.

A pyosalpinx develops through the collection of pus in the tubes which becomes distended and retort-shaped (bent) following infection, the blocked tube confines serous fluid and is referred to as a hydrosalpinx. The initial leakage of pus into the peritoneal cavity may cause acute pelvic peritonitis.

Spread of infection to the ovary binds it closely to the tube and is called a salpingo-oophoritis, and may result in the formation of a combined tubo-ovarian abscess. A collection of pus in the pouch of Douglas (peritoneum-lined space between uterus and rectum) is called a pelvic abscess.

Diagnosis is based on the following :-

1. Abdominal Examination
   - lower abdominal pain with guarding
   - rebound tenderness (parietal peritoneal involvement)
   - abdominal distension

2.	Vaginal Examination	- cervical tenderness - vaginal discharge - uterine tenderness - tenderness over tubes
3.	Investigations	- organisms isolated from cervical discharge - laparoscopy is the only definitive diagnosis - serosal swabs

Differential Diagnosis – Implications for the Herbalist

Appendicitis pain is usually central then radiating to the right iliac fossa; the fever is lower

Ruptured Ectopic Pregnancy faintness and shoulder tip pain if there is intra-peritoneal bleeding.

Unilateral tenderness and positive pregnancy test.

No pyrexia

Ovarian Tumour Torsion: pain is localised and unilateral. Pregnancy test is negative and no pyrexia.

Confirmed by ultrasound

Pyelonephritis pain associated with loin tenderness with pus cells in urine

Intestinal Obstruction usually associated with colicky pain and abdominal distension. X-Rays show fluid levels

(Adapted from : Chamberlain & Hamilton-Fairley, 1999)

Clinical Features (xref. Differential Diagnosis)

- bilateral lower abdominal pain
- fever
- deep dyspareunia (painful intercourse)
- vaginal discharge

Important Points :

* Salpingitis is never unilateral unless one tube has been removed

* Swabs from the fimbrial ends of the tube & pouch of Douglas sent for microbiological tests (cultures) for Chlamydia antigen

* Swabs from the lower genital tract (vagina, cervical canal, urethra) sent for microbiological tests for Neisseria and Chlamydia antigen

Acute Episodes vs Chronic Condition

Chronic salpingitis is usually a sequel to acute or subacute infections (see clinical features), but is associated with a low grade purulent organism eg. chlamydia. Chronic cases present with fibrosis of the fallopian tubes and inactive adhesions associated with persistent recurrent episodes of lower abdominal pain. Additional features incl. :-

Pathology	**Symptoms**
1. thickened fallopian tubes	1. lower abdominal pain
2. fibrosis	2. deep dyspareunia
3. hydrosalpinges	3. congestive dysmenorrhoea
4. pelvic floor peritoneal adhesion	4. heavy periods
5. subfertility	

Investigations Pelvic Endoscopies include the following :-

Laparoscopy Solid, metal telescope incorporating fibreoptic illumination used. Inserted into abdomen by small incision with a 2nd probe connected to a closed-circuit TV monitor that enables explorations and occlusions (through injection of a dye).

Enables surgery using instruments passed through the endoscope.

SalpingoscopySpecific endoscopic examination of the mucosa & lumen of the fallopian tubes prior to any surgery. Enables detailed examination of the widened section (ampullary segment) of the tubes for adhesions, lesions or blockage.

Hysteroscopy Specific endoscopic examination of the ostia (opening) of the fallopian tubes – assessment / extent of blockage, lesions, inflammation etc…..

Orthodox Treatment

Early diagnosis & treatment are VITAL to preserve the functional integrity of the fallopian tubes. Consequence of poor or late diagnosis and treatment may result in not only loss of fertility but damage to surrounding structures and the need for radical intervention becomes ever more pressing. Operations to restore fertility by restoring tubal patency and tubo-ovarian anatomy have limited success. Such operations must be carried out in a quiescent phase of the disease under antibiotic cover. Orthodox management falls into three categories :

1. Conservative

2. Radical / Surgical Intervention

3. Preventative Measures

Treatment rationale is dependent on:

- Aetiology
- Severity of clinical features
- Assoc. symptoms & complications
- Implications for fertility

Conservative

a) Antibiotics – Broad-spectrum (eg. Tetracyclines: Augmentin, Cephradine, Flagyl)

b) Rest

c) Analgesics

d) IV Infusion

Radical

a) Total Hysterectomy & Bilateral Salpingo-oophorectomy ('Pelvic Clearance') followed by oestrogen replacement therapy

b) Surgical drainage of pus in acute cases with pelvic Abscess

POINTS FOR CONSIDERATION : IMPLICATIONS FOR THE HERBALIST

Case History Taking: -Emphasis on previous history of PID

-Ascertaining severity & treatments of previous episode(s)

-Relevance to current complaint

Differential Diagnosis

On a cautionary note, it is important to state that the diagnosis of chronic PID is NOT clear-cut

PID is one of the most frequently pronounced, unconfirmed & erroneous gynaecological diagnoses made

Diagnosis should remain open until laparoscopy is conducted, with bacteriological investigatons / examination of

a) swabs taken from the pouch of Douglas, the fimbrial ends of the tubes and any free fluid in the peritoneal cavity
b) triple swabs (high vaginal, cervical & urethral

If in doubt…… refer !!!

Chronic pelvic discomfort may result from inactive adhesions

Lower abdominal pain in pelvic area where pelvic organs appear completely healthy suggest an underlying psycho-sexual dysfunction…..refer !!

Infertility

Most common cause of tubal disease is PID

Consider this in any consultation with presentation of infertility (importance of infertility)

confirm diagnosis of salpingitis / tubal damage if treatment for infertility is to be considered

Assess extent of damage in any previous episodes of PID prior to assessment of herbal treatment choices:

- tubal damage may have been irreversible
- radical surgery may have involved complete removal of reproductive organs

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