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HERBAL DRUGS IN BENIGN PROSTRATE HYPERPLASIA (BPH). A CURRENT UPDATE

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Keywords:

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ABSTRACT: Introduction: Benign prostatic hyperplasia (BPH) is a common age-related burden of males and found in more than 40% of men in their fifties. In Ayurveda, Vatasthila and Mutragranthi are condition mentioned under Mutraghata much resembles obstructive uropathy due to BPH. In modern medicine, management of benign prostatic hyperplasia (BPH) is either by surgical approach or by hormonal therapy and alpha-blocker *etc*. which has many complications. Thus, there is a need to update of herbal medications for treatment of BPH. The presented review article provides information on BPH and its treatment by herbal drugs. **Materials** and **Methods:** This review work was carried out by using a widespread and planned data mining approach through a search of the english-language literature indexed on Medline, Pubmed Central Journal Literature, scopus, web of science, google scholar, science direct and the proceedings of scientific meetings. To achieve significant literature author uses the key words "herbal drugs in BPH", "benign prostatic hyperplasia" "role of Ayurveda in BPH" and "current update for BPH Treatment. **Results:** nine publications were included in the final selection after systematic analysis. **Conclusion:** shigru (*Moringa oleifera* Lam), varuna (*Crataeva nurvala*), punarnava (*Boerhaavia diffusa*), gokshura (*Tribulus terrestris*) and other compound preparation of Ayurveda like Kanchanara Guggulu, Chandraprabha vati *etc*. has shown significant effect on BPH by its anti-inflammatory and antiseptic effect on genito-urinary tract.

INTRODUCTION: In the earlier phase of the disease BPH is characterized by an increase in the number of nodules, in the later phase, a significant increase in nodule volume occurs [1].

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Benign prostatic hyperplasia (BPH) is a condition due to anatomical changes in the prostate gland later affects voiding function of ageing men. BPH is a progressive disease that is commonly linked with symptoms of lower urinary tract symptoms (LUTS) such as frequent urination, urgency, nocturia, decreased and intermittent force of stream and the feeling of incomplete bladder emptying [2].

The term BPH refers to mainly histological condition such as presence of stromal glandular hyperplasia inside the prostate gland [3].

Symptoms of benign prostatic hyperplasia (BPH) are usually present after 40 years of age [4]. Volume of the prostate gland starts to increase by 2.4 cm^3 per year after the 40 years in male 5 and prostate growth rate is 2.0% to 2.5% per year in older men [6-7]. Benign prostatic hyperplasias (BPH) is generally not a life threatening condition but it can have a noticeable effect on a patient's quality of life (QOL) [8-9].

1.1 Incidence: Symptoms of BPH are rarely occurring before the age of 40 years. Moderate to severe symptoms occur in 40% of men by the age of 60 years and 80% of men by 80 years of age. Nearly all men develop BPH at the age of 90 years [10-11]. Incidences of lower urinary tract symptoms (LUTS) also increased among older men. In this context, several studies reported that it ranges from 15% to 60% in men in their 40s and 70s, respectively [12-13]. LUTS have been shown to affect more than 70% of men older than 80 years [14].

1.2 Risk Factors: There are many risk factors related to development of benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS) such as-

- **Sex Steroid Hormones:** Multiple studies have explored links of sex steroid hormones (testosterone, di-hydrotestosterone (DHT) and estrogen) with BPH and LUTS. Increased risk of BPH with increased serum concentrations of DHT and its metabolites [15-16-17].
- **Genetics:** Gene polymorphisms have been concerned in the development of BPH. Many studies showed that increased risk of symptomatic BPH and LUTS when deletions of Glutathone S-transferase enzyme genes [18]. Another study demonstrated that 16-fold risk of BPH in the presence of the prostate specific antigen (PSA) G-158A single nucleotide polymorphism [19].
- **Obesity:** Increase obesity is definitely associated with increase prostate volume. One study showed that obese male (BMI ≥ 35 kg/m 2) had a 3.5-fold increased risk of BPH as compare to non-obese (BMI <25 kg/m 2) male [20].
- **Physical Activity:** Increased physical activity and exercise reduced the risk of BPH or LUTS. Sedentary life-style is very important risk factor for development of BPH or LUTS in older age [21-22].
- **Diet:** Multiple studies have explored strong links of diet and risk of BPH or LUTS in older age. Increase use of fat, milk, alcohol consumption, dairy products, cereals and bread increase the risks of symptomatic BPH and LUTS [23-24]. Risk of BPH and LUTS are less when concentrations of vitamin E, lycopene and carotene are more in body [25-26].

1.3 Symptoms: Main symptoms of benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS) are-

- Urgency.
- Frequency.
- Nocturia.
- Dribbling (including after micturition).
- Feeling of incomplete bladder emptying.
- Urinary retention.

International Prostate Symptom Score (IPSS): The IPSS is recommended as a symptom scoring instrument to be used for baseline assessment of the severity in each patient presenting with prostatism / LUTS [27]. The grades are done on the symptom score index for the assessment of the therapy. This cannot be used to establish the diagnosis of BPH.

1.4 Diagnosis:

- Digital rectal examination (DRE). For assess the size of the prostate.
- Urine analysis for routine and microscopic examination.
- Ultrasound (KUB), trans rectal ultrasound (TRUS).
- Histological examinations like biopsy, FNAC *etc*.
- PSA assay are recommended as a marker for diagnosis and improvement after treatment.
- **Prostate Specific Antigen (PSA) Test:** PSA is most important investigation for diagnosis and used as marker to differentiate men with BPH from prostate cancer.

- Prostate specific antigen (PSA) is also used as marker of efficacy of therapeutics. PSA is in two forms that is major-bound form and minor-free form. In carcinoma of prostate, major bound form of PSA will increases and in BPH minor form of PSA will increases [28].

1.5 Treatment: In modern medicine management of Benign Prostatic Hyperplasia (BPH) is either by surgical approach such as open prostatectomy, transurethral resection of the prostate, cryotherapy *etc*.) or by conventional treatment by using hormonal therapy and alpha-blocker *etc*. Hormonal therapy has many complications such as gynecomastia, loss of libido and impotence *etc*. Treatment with an alpha-blocker or a 5α-reductase inhibitor can ameliorate symptoms and improve urinary flow rate [29-30-31] and finasteride substantially reduces the risk of acute urinary retention and the need for surgical treatment [32, 33, 34]. In a surgical technique, prostatectomy is best choice, but it also has many complications like retrograde ejaculation, postoperative morbidity and impotence, *etc*. other important surgical procedure is Transurethral Resection of the Prostate (TURP), which also have many complications [35]. Because of the limitations of the existing medical therapies and invasive therapies literally millions of elderly males are following the strategy of "watchful waiting" for the condition Benign Prostatic Hyperplasia (BPH) worldwide.

1.6 Benign Prostatic Hyperplasia (BPH) in Ayurveda: In all Ayurvedic texts, a variety of mutrarogas and their management are described which covers most of the pathological entities of the urinary system. Total 12 types of mutraghata are mentioned by Acharya Sushruta [36] and 13 types by Acharya Charaka [37]. Mutraghata comprises of two different words, that is, "mutra" means urine and "aghata" means obstructive pathology. The main features of mutraghata such as retention of urine and pain in supra-pubic region are observed due to obstruction at outlet so it can be correlated with BPH on the basis of its. Vatasthila and mutragranthi are condition mentioned under mutraghata much resembles obstructive uropathy due to enlarged Prostate on the basis of symptomatology. Vatasthila is a condition in which due to apana vayu vitiation produces movable, prominent and extremely painful glandular swelling which obstructs the passage of urine [38, 39, 40]. Mutragranthi is a small rounded and fixed glandular swelling develops all of sudden at the Vastimukha causing sudden obstruction to urine and gives rise to symptoms as like Ashmari [41]. Therefore, the disease BPH may be correlated very closely to Vatasthila by both surgical anomaly and symptoms wise.

2.0 Methodology: This review work was carried out by using a widespread and planned data mining approach through a search of the English-language literature indexed on Medline, Pubmed Central Journal Literature, scopus, web of science Google scholar, science direct and the proceedings of scientific meetings. To achieve significant literature author uses the key words "herbal drugs in BPH", "benign prostatic hyperplasia", "role of Ayurveda in BPH and current update for BPH Treatment. Inclusion criteria were literature sources such as peer reviewed journal articles, UGC care list journal, conference/ seminar proceedings book, refereed books and abstracts.

3.0 Observation: Total nine publications were included in the final selection after systematic analysis for treatment of BPH by different herbal drugs and compound preparation of Ayurveda.

3.1 Herbal Medicine used in Treatment of Benign Prostatic Hyperplasia (BPH): According to WHO, 80% of world's population depends on herbal medicines for their primary health care [42]. Natural medicines have a long history of use in India to support best possible prostate health [43]. Herbal medicines have been considered as an important option for prevention and treatment of BPH. Very limited number of herbal medicine and compound medicine of Ayurveda show efficacy against benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS) by its inflammatory and anti septic properties.

A. Varuna (*Crataeva nurvala*): The decoction of bark skin or roots in beneficial in urinary calculi, dysuria and cystitis. The decoction of bark skin or roots in beneficial in urinary calculi, dysuria and cystitis. Important formulations of varun are varunadi kwath varunadi churna *etc*. and its main therapeutic uses are in Ashmari, Mutrakricchra and Vidradhi. Decoction of *C. nurvala* increases the

force of contraction and reduces the volume of post void residual urine (PVRU) in patients with prostatic hypertrophy [44]. It minimized the tubular damage and reduced crystal deposition in the kidneys [45]. *Crataeva nurvala* reduces the risk of stone formation in experimental lithogenic animals by preventing oxalate and crystal-induced per-oxidative changes in renal tissues and increase urinary excretion of oxalate associated with reduction in citrate and glycosaminoglycans [46]. Chloroform extract of stem bark of *C. nurvala* found to be effective against both gram positive bacteria (*B. cereus*) and gram negative bacteria (*E. coli*) mediated urinary tract infection [47]. PR-2000 (*C. nurvala* containing herbal formulation) at a dose of 2 tablets thrice daily for six months showed improvement in peak flow rate (PFR) of urine and a subsequent decrease in sonographic size of prostate in human volunteers with benign prostatic hyperplasia (BPH) [48]. *C. nurvala* is main ingredient of Himplasia (herbal formulation from Himalaya Company) which was found to possess 5-α-reductase inhibitory and α-adreno receptor antagonist activity. 5-α- reductase inhibition block the conversion of testosterone to dihydro-testosterone, the major hormone in prostatic cells responsible for BPH [49]. Administration of aqueous extract of *C. nurvala* showed protective activity against ethylene glycol induced nephrotoxicity [50].

B. Shigru (*Moringa oleifera* Lam): It have potent antibacterial and antifungal efficacy. In microbial study it was found effective in case of *E. coli* followed by *S. aureus*, *K. pneumoniae*, *P. aeruginosa* and *B. subtilis*. Inhibition of fungi was also observed as more inhibition of *A. niger* was found followed by *A. oryzae*, *A. terreus* and *A. nidulans*.

The antimicrobial activity and antifungal activities of steam distillate of *M. oleifera* might be possibly due to the essential oil fraction of the plant material present in the distillate fraction [51]. Aqueous extract *M. oleifera* have anti-inflammatory action in rats [52]. Supplementation with aqueous and alcoholic extract of *M. oleifera* root-wood significantly reduced the elevated urinary oxalate, showing a regulatory action on endogenous oxalate synthesis. Thus, the results indicate that the root-wood of *M. oleifera* is endowed with anti-urolithiatic activity [53].

C. Gokshura (*Tribulus terrestris*): *Tribulus terrestris* have diuretic properties due to large quantities of nitrates and essential oil present in its fruits and seeds. The aqueous extract of *Tribulus terrestris*, elicited a positive dieresis. The increased tonicity of the smooth muscles, which was produced by *Tribulus terrestris* extract, together with its diuretic activity helped in the propulsion of stones along the urinary tract [54]. *Tribulus terrestris* was found to inhibit stone formation in various models of urolithiasis using sodium glycolate and ethylene glycol [55]. The antiurolithic activity of *Tribulus terrestris* is attributed to its glycolate oxidase inhibition. Ethanolic extract of *Tribulus terrestris* inhibits the expression of mediators related to inflammation and expression of inflammatory cytokines, which has a beneficial effect on various inflammatory conditions [56]. The alcoholic extract of *Tribulus terrestris* was found to be most active against gram positive and gram negative bacteria, while moderate activity was observed in its petroleum ether extract and chloroform extract [57].

D. Punarnava (*Boerhaavia diffusa*): Many experimental studies showed that treatment with B. *diffusa* significantly decreases the prostate weight and prostatic index in rat. Prostatic index is one of the important markers of disease, which is calculated by prostate weight to body weight ratio [58]. *In-vitro* study implies that herbal extracts has valuable effect on prostatic smooth muscle, which would relieve the urinary symptoms of disease. *B. diffusa* extract have its reported anti-inflammatory and anti-proliferative activity.

E. *Kanchanara guggulu*: *Kanchanara guggulu* is used for all types of excessive growth of various tissues including prostate gland. Kanchanara guggulu is an Ayurvedic compound formulation having properties of Vata-Kapha Dosha shamak, Lekhana (Scraping) and Shothahara (anti-inflammatory) [59]. Due to these properties, Kanchanara guggulu may use for changes of prostatic tissues and regulates the urinary function [60]. The drug Kanchanara guggulu has helped to enhance the function of the bladder. Its main ingredients are Kanchanar (*Bauhinia variegate*), Guggulu resin, Haritaki, Bibhitaki, Amalaki, Varuna (*Crataeva nurvala* bark) *etc*.

F. Chandraprabha Vati: Its main ingredients are Purified Shilajit (Black bitumen), Purified Guggulu, Karpoor, Musta, Guduchi, Daruharidra *etc*. One experimental study on rat showed that Chandraprabha vati has anti-inflammatory activity by inhibition of COX and prostaglandin mechanisms in benign prostatic hyperplasia [61].

CONCLUSION: BPH is a common age-related affliction of males and is the most common neoplastic abnormality in men. Histological evidence of BPH can be found in more than 40% of men in their fifties. One in four males will undergo surgery at some time in their life to relieve symptoms of BPH. BPH is a progressive disease that is commonly linked with symptoms of lower urinary tract symptoms (LUTS) such as frequent urination, urgency, nocturia, decreased and intermittent force of stream and the feeling of incomplete bladder emptying. BPH is a slow progressive disease and its management is either by conservative methods or surgical methods. Prostatectomy *i.e.* surgical removal of prostate gland is a golden treatment for BPH but it is associated with many complications like post operative morbidity, impotence, retrograde ejaculation *etc*. Vatasthila and mutragranthi are condition mentioned under mutraghata much resembles obstructive uropathy due to enlarged Prostate on the basis of symptomatology. Very limited number of herbal medicine and compound medicine of Ayurveda show efficacy against benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS) by its inflammatory and anti septic properties. Decoction of *C. nurvala* increases the force of contraction and reduces the volume of post void residual urine (PVRU) in patients with prostatic hypertrophy. Aqueous extract *M. oleifera* have anti-inflammatory, antibacterial and anti fungal action in rats. *Tribulus terrestris* have diuretic properties due to large quantities of nitrates and essential oil present in its fruits and seeds. *B. diffusa* significantly decreases the prostate weight and prostatic index in rat. Kanchanara guggulu is used for all types of excessive growth of various tissues including prostate gland. Chandraprabha vati have anti-inflammatory activity by inhibition of COX and prostaglandin mechanisms in benign prostatic hyperplasia. By the use of herbal drugs and compound ayurvedic formulation BPH and LUTS can be easily manage without any side effect or with minimum side effect.

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