

Comparative Acute Oral Toxicity Study of Verona Anti-BPH with Verona Max in Mice

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ABSTRACT

Authors' Contributions

1 Conception & Study Design, Data Analysis, Drafting, Critical Analysis.
2,5,7 Data Collection, Data Analysis, Drafting.
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Objective: Benign Prostate hyperplasia (BPH) is hyperplasia of prostate gland and age related diseases in men. 20%-60% men have BPH with the age of 40 to 60 years. The cause is not very well researched however the pharmacological and surgical current treatments have numerous toxic effects on quality of life. Natural medicines are known for its safety as compare to pharmacological choice of medicines. By considering this fact, current experimental study was established to compare and assess the acute oral toxicity of the Verona Anti-PBH with Verona Max in NMRI strain of mice on animal model.

Methodology: NMRI mice were obtained for experimental purpose from animal house facility of Herbion Pvt. Ltd. Constant environmental conditions were 25 ± 1 °C with R.H 52 - 61% with 12 hours dark and light cycle. As per desire, food and water were available. Animals were divided into three different groups including two treatment and control group. Treatment group including Verona Anti-BPH and Verona Max however control group were on water. Animal's age were 6-8 weeks and average body weight were 25-35 g however cage cards were used for identifications between the groups. Mice were treated orally using gastric gavage with doses (1 or 5g/kg) of test product for 14 days and observed daily.

Results: The Verona anti-BPH and Verona Max did not cause any sign of ill health and acute toxicity in mice at the given doses of 1 or 5 g/kg. No hair loss, color loss, heart rate (chest expansion and retraction), writhing, stretching and fecal abnormality was observed. No remarkable change in the behavior and no mortality was observed.

Conclusion: The present study evaluated that Verona anti-BPH and Verona Max extract is potentially safe and no acute oral toxicity has found.

Keywords: Benign Prostate Hyperplasia (BPH), verona, acute oral toxicity, herbal remedy.

INTRODUCTION

Benign Prostate Hyperplasia (BPH) is actually the hyperplasia of prostate gland. This is strictly age related diseases in men and starts approximately at the age of 40 years. As per prevalence rate of BPH, it was concluded by autopsy that 11% men have BPH at the age of 30 years, 20% have on 40 years, and

50% to 60% men have at the age of 60 years however 80% to 90% have on the age of 70 to 80 years. The histological feature consistent with age at the condition of BPH [1, 2]. As per the definition of International Classification of Diseases (ICD), BPH not produces problem to the patient necessarily and create urge for visit of the particular cause [3].

After many experimental studies and human researches, the cause of BPH is still unknown. It has proven that the hormone Androgens is important for the growth and development in men [4, 5]. However, a weak correlation found between urodynamic observation and urinary symptoms. These diseases decrease the urine flow which ultimately increases the pressure of detrusor muscles and cause severe pain [6-8]. For minimize the pain and symptoms three different types of treatments were recommended including watchful awaiting, pharmacological and surgical [9].

Natural medicine are known for its minimum side effects however it was estimated that the cost of herbal medicine consumptions are over 3.5 billion annually by American population [10, 11]. Multiples researches have proved that the holistic and traditional medicines are preventing and treating the disease related to prostate [12]. As the practicing surgical processes are very painful so it's a need of time to think about the natural medicine which can ultimately improve the quality of life with minimum toxic effects. Verona Anti-BPH is a combination of the herbal ingredients including *Saw palmetto*, *Stinging nettle*, *Cucurbita pepo*, *Pygeum africanum* and Nocturia. *Lycopene*. However, Verona Max contains *Lepidium meyenii*, L-Argenine, *Epimedium* and standardized extract of *Tongkat ali*, Horney goat weed and *Tribulus terrestris*. It acts as a potent aphrodisiac for the management of pre-mature ejaculation and erectile dysfunction.

The herb "Saw palmetto" has been used extensively for BPH throughout Europe [13, 14]. The active component of the herb is still unclear but its shows anti-inflammatory effect, blocked testosterone to dihydrotestosterone and involution of prostate epithelial gland [15]. *Urtica dioica* L. also called Urticaceae, used a folk medicine and mechanically inhibit cell proliferation of Hela cells and block the binding of epidermal growth factors (EGF) for producing inhibiting effects on the treatment of BPH [16]. *Cucurbita pepo* (Pumkin) is used for numerous diseases include anti-inflammatory, anti-viral and analgesic urinary disorders. Traditional Ayurveda and Chinese system used its plant, fruit and seed for healing of wounds and inhibition of tumor growth. It has strong effects on alleviate prostate diseases and kidney stones [17]. *Pygeum africanum* also recovers urodynamic in the condition of benign prostate hyperplasia [18]. *Lycopene* helps to reduce prostate

cancer risk, proliferation of cancerous cells, reducing DNA damage and improve oxidative stress [19].

The *Lepidium meyenii* (Maca) creates effects on seminal analysis including increased seminal volume, increase sperm count per ejaculum, increase motility of sperm without modification in sexual hormones and increase motile sperm count [20]. Tongkat ali helps to improve male fertility, helps to increase motility and spermatozoa count [21]. Horney goat weed is also help to improve erectile dysfunction [22], however *Tribulus terrestris* helps to improve fertility, libido and helps to improve spermatogenesis [23].

The aim of the current research is to compare and evaluate the acute oral toxicity between Verona Anti-BPH, Verona Max and control group.

METHODOLOGY

For evaluation of acute oral toxicity, selected animals were NMRI mice from the animal's house facility of Herbion Pakistan Pvt. Ltd. Animals were divided into three different groups, first group was taking Verona anti BPH, second group were on Verona Max however third group were on water as a control group. Experimental animals were kept under constant environmental conditions i.e. $25 \pm 1^\circ\text{C}$, relative humidity (RH) 52 - 61% with 12 hours night and day cycle. Food and water were available *ad libitum*. Age of the animals and body weight were 6-8 weeks and 25-35g. Body weights of these mice were taken after the initial stabilization period. Cage cards were used for identification between two groups. After initial weight, animals were randomly distributed into each group. No randomization pattern was selected. The experiments were carried out in the premises of the conventional animal house facility of the Herbion Pak. Pvt. Ltd. and ethical approval has been taken from Jinnah University for Women Karachi.

For evaluation of acute oral toxicity evaluation, animals were evaluated on physical and behavioral examination, mortality and morbidity, food intake and body weight changes. Mice were treated orally using gastric gavage with doses (1 or 5g/kg) of test product for 14 days and observed daily.

RESULTS

On Physical examination, The Verona anti-BPH and Verona max did not produce any untoward effects on health or create any toxicological effects in mice at

the given doses of 1 or 5 g/kg. No hair loss, Abdominal Palpitation, Genital Abnormality, color loss, heart rate (chest expansion and retraction), and writhing, stretching and fecal abnormality was observed as shown in Table 1.

All experimental groups did not produce any remarkable change in behavior including normal locomotive and socialization activities as shown in Table 2.

Table 1. Physical examination.

Drugs	Physical Examination								
	Hair Loss	Abdominal Palpitation	Genital Abnormality	Color Loss	Abnormal Heart Rate	Writhing	Abnormal Stretching	Fecal Abnormality	Abnormal Respiration
Control (Water)	No	No	No	No	No	No	No	No	No
Verona Anti-BPH (Extract)	No	No	No	No	No	No	No	No	No
Verona Max (Extract)	No	No	No	No	No	No	No	No	No

Table 2. Behavioral examination.

Drugs	Behavioral Examination											
	Social Interaction	Alertness	Grooming	Restlessness	Touch Response	Aggression	Pain Response	Convulsions	Tremors	Lacrimation	Salivation	Corneal Reflex
Control (Water)	Normal	Normal	Normal	No	Normal	No	No	No	No	No	No	Normal
Verona Anti-BPH (Extract)	Normal	Normal	Normal	No	Normal	No	No	No	No	No	No	Normal
Verona Max (Extract)	Normal	Normal	Normal	No	Normal	No	No	No	No	No	No=	Normal

Table 3. Mortality and morbidity.

S. No.	N (Male)	Test Substance	Dose Level (mg/kg)	Mortality (%)
1	10	Verona Anti BPH (Extract)	1000	0
			5000	0
2	10	Verona Max (Extract)	1000	0
			5000	0
3	10	Control (Water)	1000	0
			5000	0

Table 4. Changes in body weight.

Drugs	Species	Dose (mg/kg)	Animals (N)	Body Weight (Day=0) Mean±S.D	Body Weight (Day=7) Mean±S.D	Body Weight (Day=14) Mean±S.D
Control (Water)	Mice: NMRI strain	1000	10	29.6±0.426	30.4±0.426	30.6±0.520
		5000	10	29.6±0.520	29.4±0.4	29±0.494
Verona Anti-BPH (Extract)	Mice: NMRI strain	1000	10	29.4±0.791	29.2±0.8	28.8±0.952
		5000	10	28.8 ±0.997	28.4±1.146	28.1±1.129
Verona Max (Extract)	Mice: NMRI strain	1000	10	25±0.954	24.8±1.162	24.8±1.162
		5000	10	26.1±0.959	25.8±1.123	25.6±1.212

No mortality and morbidity was observed with doses of 1 and 5 g/kg of Verona anti-BPH extract and Verona Max including control group (Table 3).

No significant difference between food intake of treated and control groups was noted. Body weights of each animal recorded prior to the test item administer on day 0 and after administration of drug on day 7 and 14. No Significant changes in weight were observed between all 3 groups as shown in Table 4.

DISCUSSION

BPH is rarely life threatening diseases which creates huge impact on quality of life parameters. Many treatments are available including transurethral incision and resection however pharmacological treatment approaches are available including popular drug finasteride [24]. Many side effects have been reported including ejaculation disorder libido, hair loss, depressive with suicidal symptoms [25]. Due to the need of time, Verona max has been developed. The results have been showed that no impact on physical examination including hair loss, aggression etc. However, it has also proven that no effect was observed on behavioral examination mortality and morbidity. No changes have been observed in body weights of animals as well.

CONCLUSION

The present study demonstrated that the Verona anti-BPH powdered extract is potentially safe. No

abnormality on physical examination, behavioral examination has been observed. No mortality and morbidity has been seen and no significant weight increase/ decrease has been observed as compare to the control (water). By seeing the facts and figures, Verona Max and Verona Anti BPH (extracts) considered to the effective medication as compare to the marketed brands with no hair loss, no suicidal and depressive symptoms.

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