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Lauric acid and myristic acid prevent testosterone induced prostatic hyperplasia in rats

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ABSTRACT

Numerous plants have proven to improve uncontrolled growth of the prostate gland and improve urinary tract symptoms associated with benign prostatic hyperplasia. Major components of those plants were lauric acid and myristic acid. Our study investigated whether lauric acid or myristic acid prevent testosterone induced prostatic hyperplasia in rats. Rats were divided into negative control and testosterone induced prostatic hyperplasia rats (positive control, low dose lauric acid treated, high dose lauric acid treated, low dose of myristic acid treated, high dose of myristic acid treated, finasteride treated). Testosterone and drug treatment were carried out for 14 days. Body weights were recorded before and after treatment. On 15th day, rats were sacrificed, prostates were weighed and histopathological studies were carried out. Lauric acid/myristic acid treatment showed significant inhibition of prostate enlargement and protection of histoarchitecture of prostate when compared with positive control group. In conclusion, the study showed that lauric acid/myristic acid reduced the increase of both prostate weight and prostate weight:body weight ratio, markers of testosterone induced prostatic hyperplasia in rats.

1. Introduction

Benign and uncontrolled growth of the prostate is benign prostatic hyperplasia. (Arruzabala et al., 2006). It is a common condition in elderly men, with an estimated prevalence of up to 85 % (Slaa et al., 1997). Benign prostatic hyperplasia is multifactorial disease, a most common noncancerous form of abnormal prostate cell growth (Gossel and Wuest, 2004). Benign prostatic hyperplasia is characterized by lower urinary tract symptoms like urinary frequency, urgency, weak and intermittent stream, needing to strain, a sense of incomplete emptying and nocturia and can lead to complications including acute urinary retention, obstructive uropathy and urinary tract infection (Barry, 2001).

Although the etiology of benign prostatic hyperplasia is not completely elucidated, it involves hormonal changes in the aging man. The development and growth of prostate gland depends on androgen stimulation, mainly by dihydrotestosterone (DHT), an active metabolite formed due to enzymatic conversion of testosterone by steroid 5α-reductase. Production and accumulation of DHT in the prostate increases with aging which results in encouraging cell growth and induction of hyperplasia (Carson and Rittmaster, 2003; Bartsch et al., 2000). Benign prostatic hyperplasia also involves augmented adrenergic tone in prostate smooth muscle, regulated through α_1-adrenoceptors (Michel et al., 1998).

Conventionally used drugs like steriod 5α-reductase inhibitors (finasteride and dutasteride), α -adrenoceptor antagonists (alfuzosin, doxazosin, tamsulosin, terazosin) are used to treat benign prostatic hyperplasia, but they possess various side effects like impotence, decreased libido, ejaculation disorder, gynaecomastia, dizziness, upper respiratory tract infection, headache, fatigue, and additional responses were reported in post marketing investigation which includes rash, tachycardia, and chest pain (Patel and Chapple, 2008). Along with conventional therapy, some alternative therapies are also available to treat prostatic hyperplasia.

Various *in vitro* studies have reported that fatty acids inhibit the enzyme 5α-reductase enzyme activity (Liang and Liao, 1992; Niederprum et al., 1994; Raynaud et al., 2002). Herbal drugs like *Serenoa repens* (Plosker and Brogden, 1996; Weisser et al, 1996; Lowe et al., 1998; Wilt et al., 2000; Aliaev et al., 2002; Carbajal et al., 2005), coconut oil (Arruzabala et al., 2006) had proven to be effective in benign prostatic hyperplasia. The mechanism contributing for their protective effect against prostatic hyperplasia is mainly due to 5α-reductase inhibitory activity, which is due to their high content of lauric acid and myristic acid (mainly lauric acid).

However, there is no evidence for efficacy of lauric acid/myristic acid on testosterone induced benign prostatic hyperplasia in rats. Hence in the present study, we have investigated whether oral dosing with lauric acid/myristic acid could prevent testosterone induced hyperplasia in rats.

2. Materials and methods

2.1. Animals

Male Wistar rats weighing 180–220 g were procured from an institutional animal facility centre. They were housed individually in

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clean and transparent polypropylene cages maintained at room temperature with 12-h light/dark cycle and had free access to food and water. After 7 days of acclimatization, they were randomly distributed into experimental groups.

All the experimental procedures were carried out in accordance with Committee for the purpose of control and supervision of experiments on animals (CPCSEA) guidelines. The study was reviewed and approved by the Institutional Animal Ethics Committee, K.L.E.S, College of Pharmacy, and Belgaum, India.

2.2. Chemicals

1) Lauric acid (Sigma-Aldrich Pvt Ltd)
2) Myristic acid (Sigma-Aldrich Pvt Ltd)
3) Finasteride (FINAST, Dr. Reddy's Laboratories)
4) Testosterone propionate (courtesy of Genesis Pharmaceuticals, Japan)

2.3. Administration and dosage

Fatty acids were suspended in distilled water by using Tween 80 and administered orally. Testosterone propionate was diluted with distilled water using Tween 80 as emulgent and injected subcutaneously (3 mg/kg) daily for 14 days. Rats were divided into seven groups (six rats each). A negative control group (Group I) received vehicle orally and six groups were injected testosterone subcutaneously (3 mg/kg) to induce prostatic hyperplasia (PH) (Arruzabala et al., 2006). These six groups were further divided into positive control (Group II), finasteride: 5 mg/kg (Group III), lauric acid: 180 mg/kg (Group IV), lauric acid: 360 mg/kg (Group V), myristic acid: 70 mg/kg (Group VI), myristic acid: 140 mg/kg (Group VII) groups.

2.4. Body weight

Animals were weighed before initiation and after completion of the experiment.

2.5. Prostate weight

Animals were sacrificed by light ether anaesthesia and prostates were removed and weighed immediately.

2.6. Prostate weight to body weight ratio

Prostate weight to body weight ratio were calculated.

2.7. Percentage of inhibition

a) Prostate weight
b) Prostate weight/body weight ratios.

Percentage of inhibition was calculated as follows:

$$100-[(\text{treated group}-\text{negative control})/(\text{positive control}-\text{negative control}\times 100].$$

2.8. Histopathological investigation

The paired prostates were dissected free from fascia and fixed in Bouin's solution with haematoxylin and eosin stain and observed under light microscope (20×).

2.9. Statistical analysis

Data were expressed as mean ± S.E.M. Statistical analysis is done by one-way ANOVA followed by Bonferroni's multiple comparison Test. $P<0.01$ considered as significant.

3. Results

3.1. Evaluation of prostate enlargement

3.1.1. Prostate weights

Significant elevation in prostate weights was found by testosterone treatment when compared with negative control rats. But significant reduction in elevation of prostate weights was found by lauric acid and by myristic acid in testosterone treated rats. Percentage inhibition was 44.8 and 64.1 by 180 mg/kg and 360 mg/kg of lauric acid and 29.1 and 53.2 by 70 mg/kg and 140 mg/kg of myristic acid respectively when compared to negative control animals (Table 1).

3.1.2. Prostate weights to body weights ratio

Testosterone significantly elevated the prostate weights/body weights ratio when compared with negative control rats. But significant reduction in elevation of prostate weight/body weight ratio was found by lauric acid and by myristic acid in testosterone treated rats. Percentage inhibition was 49.2 and 60.1 by 180 mg/kg and 360 mg/kg of lauric acid and 20.0 and 51.6 by 70 mg/kg and 140 mg/kg of myristic acid respectively when compared to negative control animals (Table 1).

3.2. Body weight changes

There were no significant differences in body weights of rats before and after testosterone treatment among the groups (Table 1).

3.3. Histopathology of prostate

There was no change in the histoarchitecture of prostate gland in negative control group. The tissues were tightly packed, epithelium was cuboidal and regular in size (Fig. 1A). In positive control group,

Table 1
Effect of lauric acid/myristic acids on body weights and prostate enlargements in testosterone treated rats.

Sr. no.	Groups	PW (g)	% inhibition	PW/BW ratio ($\times 10^{-3}$)	% inhibition	Body weights (g)	
						Initial	Final
1)	Group I	0.310 ± 0.011	–	1.553 ± 0.01453	–	198.3 ± 10.53	204.3 ± 5.36
2)	Group II	0.603 ± 0.019[a]	–	3.048 ± 0.08146[a]	–	198.3 ± 5.578	200.2 ± 5.99
3)	Group III	0.385 ± 0.009[c]	74.40%	1.91 ± 0.01095[c]	78.30%	201 ± 4.78	204.7 ± 3.73
4)	Group IV	0.470 ± 0.012[c]	44.82%	2.283 ± 0.06254[c]	49.20%	202.8 ± 6.63	205.7 ± 3.75
5)	Group V	0.416 ± 0.009[c]	64.10%	2.097 ± 0.005578[c]	60.12%	198.3 ± 4.66	195.5 ± 4.52
6)	Group VI	0.518 ± 0.012[b]	29.10%	2.587 ± 0.1190[b]	20%	196.8 ± 4.37	190.8 ± 4.04
7)	Group VII	0.447 ± 0.0170[c]	53.20%	2.315 ± 0.09421[c]	51.60%	195.2 ± 5.55	198.5 ± 5.39

PW: prostate weight, BW: body weight, Group I: negative control, Group II: positive control, Group III: finasteride (5 mg/kg), Group IV: lauric acid (180 mg/kg), Group V: lauric acid (360 mg/kg), Group VI: myristic acid (70 mg/kg), Group VII: myristic acid (140 mg/kg). Values are expressed as mean ± S.E.M. Statistical analysis is done by one-way ANOVA followed by Bonferroni's multiple comparison test. There was no significant difference between body weights groups.

[a] $P<0.001$ when compared with normal control.
[b] $P<0.01$ when compared with testosterone treatment.
[c] $P<0.001$ when compared with testosterone treatment.