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Effects of foam-mat dried soursop smoothie powder on prostate-specific antigen and kidney function in male Albino Wistar rats

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Abstract

The effect of ethanolic extracts of foam mat dried soursop smoothie powder on Prostate Specific Antigen (PSA) and renal function of rats induced with prostatic hyperplasia, using testosterone propionate was investigated. Forty-nine rats were divided into seven groups A, B, C, and D_1 - D_4 of seven rats each− Group A received commercial rodent feed. Group B received Testosterone propionate (TP). Group C received Testosterone propionate and Finasteride (TP+F). Four groups (D_1 - D_4) received different doses of ethanol extract. At the end of experiment, the rats were sacrificed and blood was collected and serum evaluated for PSA, urea and creatinine estimation at ($p<0.05$). Result shows that while the normal PSA level is 4.0ng/ml, animals treated with TP had 9.70ng/ml, those treated with TP + F had 6.80ng/ml and those treated with TP + extract had a range of 5.13-6.00ng/ml PSA. Creatinine values of animals treated with extract ranged from 50.21-52.60mg/dl, those treated with F alone had 36.50mg/dl and the untreated group had 128.10mg/dl against the normal range of 7-12.98mg/dl. Normal serum urea ranges from 15-64.2mg/l however, animals treated with F+ extract ranged from 133.7- 189.8mg/l while untreated ones had 248.8mg/l. A progressed atypical hyperplasia was observed in the dorsolateral prostate region of rats that received Testosterone alone compared to those treated with extract after receiving TP. The response of the animals given higher dose of the extract may provide a relevant animal model for human prostatic cancer.

Keywords: Soursop ethanol extract, therapeutic assay, kidney function.

Introduction

Benign prostatic hyperplasia (BPH) is a prevalent condition in aging males, often associated with elevated levels of prostate-specific antigen (PSA), a glycoprotein produced by prostatic epithelial cells (Menez, 2008). While PSA levels between 0.0 and 4.5 ng/ml are generally considered normal, levels above this range may indicate BPH or prostate cancer, though prostate malignancies can occasionally occur without PSA elevation (Thompson, 2004). Increased prostate weight is another critical marker of BPH and pharmaceutical treatments such as finasteride have demonstrated efficacy in reducing prostate weight (Bisson, 2007). However, there remains significant interest in discovering natural products that may alleviate BPH symptoms while exerting fewer adverse effects.

Soursop (Annona muricata L.) is the largest tropical fruit of the *Annonas* genus and is renowned for its distinct aroma and flavour (Singh and Medhi 2003). It is cultivated widely throughout tropical and subtropical regions, including India, Malaysia, and Nigeria (Adewole and Caxton-Martins 2006). Traditionally, various parts of the soursop plant—leave, pulp and bark—have been used to manage conditions such as hypertension and diabetes (Badrie and Schauss 2010). More recent studies also suggest that soursop possesses anticancer properties, including toxicity against prostate

PC-3 cancer cells and potential antidepressant effects (Moghadamtousi *et al*., 20l5). Despite these recognized therapeutic attributes, there is a paucity of research specifically examining the effects of processed soursop products on BPH.

Additionally, many herbal extracts that show promise for prostate health can inadvertently affect renal function. The kidney plays a central role in excreting waste products—particularly urea and creatinine—through glomerular filtration (Okolie, 2011). If these nitrogenous metabolites accumulate, they may signal renal impairment or tubular dysfunction. While decoctions of soursop leaves have been reported to provide certain protective health benefits (Badrie and Schauss 2010), the impact of *foam-mat dried* soursop, a technique known to preserve heat-sensitive phytochemicals, remains largely unexplored in the context of both prostatic and renal health. Given these gaps, this study was designed to investigate the effects of ethanol extract from foam-mat dried soursop smoothie powder on PSA levels and renal function indices in male albino Wistar rats with testosterone propionate-induced BPH. By examining the interplay between soursop extract dose, PSA reduction and kidney function, our findings may offer insights into the therapeutic potential and safety profile of soursop-based interventions for BPH management.

Materials and Methods

Plant material and extraction

Ripe soursop (*Annona muricata L.*) fruits were purchased from Oji-River in Enugu State, Nigeria. Fruits were inspected for uniform colour and firmness. The pulp was extracted, steam-blanched for 4 minutes and subjected to foam-mat drying at 45°C in an air oven. The dried pulp was powdered and stored in airtight containers at room temperature. For the ethanol extract, 400 g of powdered soursop fruit was macerated in 2.5 L of ethanol for 24 hours. The filtrate was concentrated in a water bath at 45°C (Umeh, *et al*., 2005) and stored in a refrigerator for in vivo studies. An oral acute toxicity test was performed according to OECD (2022) guidelines. The extract was reconstituted in normal saline at required doses for animal administration.

Animal experimental design

Forty-nine male Wistar albino rats were obtained from the Laboratory Animal Unit, Faculty of Veterinary Medicine, University of Nigeria, Nsukka. They were housed in stainless steel cages, with 12-hour light cycles, and acclimatized for 7 days. Tap water and rodent feed were provided *ad libitum*. The rats were distributed into seven groups (n = 7 per group):

Group A: The rats orally received 1 ml of normal saline daily for 12 weeks in addition to having free access to commercial rodent feed and water ad-libitum.

Group B: The rats received 14mgKg-1 of Testosterone Propionate (TP) intraperitoneally for 8 weeks alternating with 2 weeks of the commercial rodent feed and water ad-libitum.

Group C: The rats received 14mgKg-1 of TP intraperitoneally for 8 weeks alternating with 2 weeks of orogastric administration of 10mgKg-1 Finasteride (F) in addition to having free access to commercial rodent feed and water ad-libitum.

Group D_1-D_4: The rats received 14mgKg-1 of TP intraperitoneally for 8 weeks alternating with 2 weeks of oral ethanolic extract of soursop smoothie powder (SSP) in doses of 1ml equivalent of 100, 200, 300 and 400mgKg-1 in addition to having free access to commercial rodent feed and water ad-libitum.

- **Group A (Control)**: Normal saline; served as negative control.
- **Group B (Positive)**: Testosterone propionate (TP) intraperitoneally to induce BPH.

- **Group C (Intermediate)**: TP + Finasteride.
- **Group D_1** : TP + 1 mL of soursop extract equivalent to 100 mg/kg body weight.
- **Group D_2** : TP + 1 mL of soursop extract equivalent to 200 mg/kg body weight.
- **Group D_3** : TP + 1 mL of soursop extract equivalent to 300 mg/kg body weight.
- **Group D_4** : TP + 1 mL of soursop extract equivalent to 400 mg/kg body weight.

After three months, one rat each was randomly selected from each group and was anesthetized with chloroform. Blood samples were collected via cardiac puncture using a 5mL syringe and centrifuged at 3000rpm for 10 minutes. Serum was stored at 4°C prior to analysis. Prostate and seminal vesicles were harvested, blotted dry and fixed in 10 % buffered formaldehyde solution for 24 hours. The tissues were dehydrated in 95 % ethanol, cleared in chloroform and embedded in paraffin wax. Sections (4 μm) were obtained using a rotary microtome, mounted on slides and stained with hematoxylin and eosin (Adeteye *et al*., 2011).

Biochemical evaluation of total prostate-specific antigen (t-PSA)

A monoclonal anti-PSA antibody and Prostate-Specific Antigen-horseradish peroxidase (PSA-HRP) conjugate system was used (Gershman *et al.,*2017). Exactly, 5mL of blood sample from the BPH-induced rats was incubated with PSA-HRP conjugate in a pre-coated plate for 1 hour. After incubation, the wells were decanted, washed and incubated with HRP substrate producing a blue-coloured product. The reaction was stopped and the absorbance read at 450 nm on a microplate reader.

Renal function test

Urea concentration was determined by the diacetyl monoxime method using a kit from Randox Laboratories (UK). Creatinine concentration was determined by the alkaline picrate method (Tietz, 2008) with slight modifications.

Statistical analysis

Data were expressed as mean ± SD of four determinations. One-way analysis of variance (ANOVA) was performed using SPSS version 25.0. Mean differences were considered significant at $P< 0.05$ (Smaga, 2024).

Results and discussion

Effect of Foam-Mat Dried Soursop Smoothie Powder Extract on Renal Function and PSA levels of rats administered with testosterone propionate (TP) and finasteride as shown in Table 1. The oral administration of the ethanolic soursop extract during the oral acute toxicity test show no signs of bizarre behaviour to suggest toxicity nor was there any record of death, or clinical signs of toxicity such as writhing, muscle paralysis or respiratory distress during the study. Howbeit, intra cavity administration of the vehicle was reported by Figueido *et al.* (2022) as a suitable route in the administration of TP. Therefore, the mortality recorded could be associated with the direct impact of the inducement and the high dose of the extract due to the presence of tissue-damaging phytochemicals which could cause irritation to the renal tissues through the deleterious effects of kidney injuries resulting in development of chronic kidney disease and mortality.

Renal function (Urea and Creatinine)

The kidney plays a critical role in maintaining homeostasis and excreting waste products, including urea and creatinine (Okolie, 2011; Agbasi *et al*., 2010). Elevated

levels of these parameters often indicate renal impairment. In healthy adult males, serum creatinine ranges between 61.01–106.99 µmol/L and blood urea nitrogen ranges between 2.22–4.99 µmol/l (Cakrawati *et al*., 2022). In this study (Table 1), rats treated with TP + Finasteride (Group C) showed significantly ($P< 0.05$) lower urea levels compared to Group B (TP alone). Administrations of 1ml equivalent of 100 and 200 mg/kg soursop extract (Groups D_1 and D_2) also reduced serum urea levels relative to Group B, albeit not as low as Group C. However, at higher doses of 300 and 400 mg/kg (Groups D_3 and D_4), urea concentrations were higher compared to D_1 and D_2, indicating changes of the cytoarchitecture of the renal cortical structures of the kidney (Zubaidi *et al*., 2023).

Serum creatinine was elevated in all TP-induced groups, reflecting possible glomerular inflammation or interstitial nephritis. While Groups D_1 and D_2 showed higher creatinine levels than Groups D_3 and D_4, both groups remained above the control level (Group A). The relatively lower creatinine levels in the D_3 and D_4 groups (300 and 400 mg/kg) might be due to the ability of extract to enhance elimination of creatinine and urea in the urine through increased urine production and synergistic effect of the phytochemical constituents (Adekunle *et al.*, 2020).

Prostate-specific antigen (PSA)

PSA is a valuable tumour marker for early prostate disease detection. Elevated PSA (>4 ng/mL) can indicate BPH or prostate cancer (McConnel, 2024; Arene *et al*., 2022). Group B (TP alone) had the highest PSA (9.70 ng/mL), suggesting a high risk of prostatic lesion. Groups D_1, D_2, D_3, and D_4 showed significantly lower PSA levels, indicating the protective or curative effect of soursop extracts. Onyegeme-Okerenta *et al*. (2022), reported a significant decreased the PSA levels of the rats in treatment groups with Testosterone propionate induced Benign Prostatic Hyperplasia treated with aqueous soursop pulp extract indicating the ameliorative impact of TP induced BPH as a result of inhibitory 5-reductase, linked to a reduction in BPH. This corroborates the findings of Ogbu *et al* (2020) who discovered acetogenin rich fraction isolate from soursop plant reduced the level of PSA in induced BPH rats. Overall, the results demonstrate that soursop ethanol extract attenuates PSA elevation and modulates renal parameters, although higher concentrations might pose some renal challenges.

Table 1: Biochemical test for renal function and PSA levels of rats treated with testosterone propionate, finasteride, and ethanolic extract of soursop smoothie powder

Group	Treatment	Effective number of rats	Urea (mg/l)	Creatinine (mg/dl)	PSA (ng/ml)
A	Normal saline	7	$93.30^{a} \pm 0.03$	$26.40^{a} \pm 0.10$	$4.60^{a} \pm 0.10$
B	TP alone	5	$248.80^{b} \pm 0.01$	$128.10^{b} \pm 0.10$	$9.70^{b} \pm 0.10$
C	TP + F	7	$133.70^{c} \pm 0.00$	$36.50^{c} \pm 0.10$	$6.80^{c} \pm 0.20$
D_1	TP+SEE(100)	7	$146.80^{d} \pm 0.01$	$52.60^{d} \pm 0.20$	$6.00^{d} \pm 0.00$
D_2	TP+SEE(200)	6	$168.90^{e} \pm 0.01$	$51.70^{e} \pm 0.20$	$5.63^{e} \pm 0.01$
D_3	TP+SEE(300)	5	$170.70^{f} \pm 0.01$	$50.58^{f} \pm 0.01$	$5.20^{f} \pm 0.10$
D_4	TP+SEE(400)	5	$189.80^{g} \pm 0.01$	$50.21^{g} \pm 0.01$	$5.13^{c} \pm 0.02$

NB: Mean ± Std values in the same column with different superscrips were significant ($p < 0.05$).
Key: A = Control group, B = Positive group, C = Intermediate group, D1- D4 = treatment with different doses of SEE, TP = Testosterone propionate, F = Finasteride, SEE = Soursop Ethanol extract.

Histopathological findings

The histological appearance of prostate gland lesions varied markedly among treatment groups. **Group A (Plate 1)** exhibited normal prostatic architecture, characterized by pinkish secretory corpora amylacea and a well-defined fibromuscular capsule, indicating healthy tissue. In contrast, **Group B (Plate 2),** administered testosterone propionate alone**,** revealed severe degeneration with severe hyperplasia leading to dilated prostatic gland with loss of prostatic secretion copra amylacca and focal area inflammation .

Rats treated with testosterone propionate plus finasteride (**Plate 3**) displayed severe degeneration with severe hyperplasia featuring dilation of the prostatic gland and diminished secretory corpora amylacca, but no focal inflammatory regions. Meanwhile, rats from the extract treated groups (**Plates 4 and 5**) showed varying degrees of degenerative hyperplasia, with glandular dilation, loss of secretory materials and cribriform patterns indicative of ongoing pathological changes.

These findings corroborate the biochemical data, showing that soursop extract—especially at specific doses—partially mitigates hyperplastic changes. Similar observations were reported by Asare *et al*. (2015), where *A. muricata* leaf extract suppressed BPH-1 cells in a rat model. Although, Leje *et al.* (2024) reported that soursop aqueous extract reduced BPH and PSA levels of experimental animals positively without any adverse effect. The presence of phenols, flavonoids, alkaloids and acetogenin may confer antioxidant and anti-tumor properties (Agu and Okolie 2017). Collectively, the current results suggest that foam-mat dried soursop extract may mitigate, though not completely resolve, hyperplastic lesions associated with testosterone propionate-induced prostate enlargement.

Plates 1-5. Shows the photomicrograph section of histological appearance of prostate gland of rats treated with Testosterone propionate, Finasteride and ethanolic extract of soursop smoothie powder (H/E)(x400).

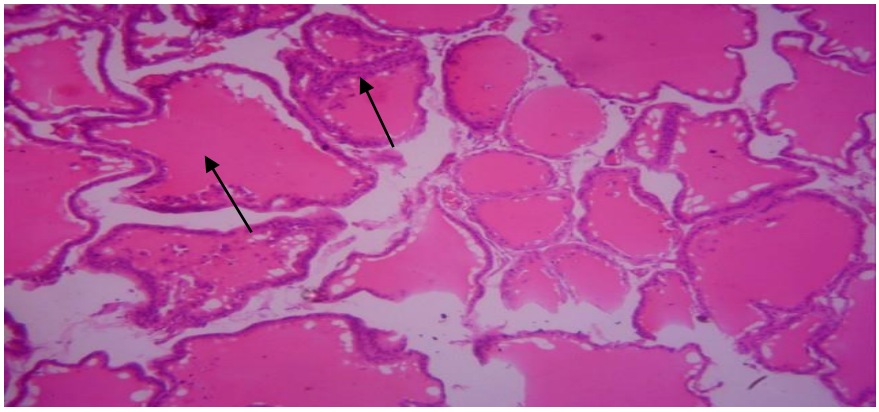


Plate 1 (Group A): Normal prostatic tissue with a fibromuscular capsule and pinkish secretory corpora amylacea (CA).

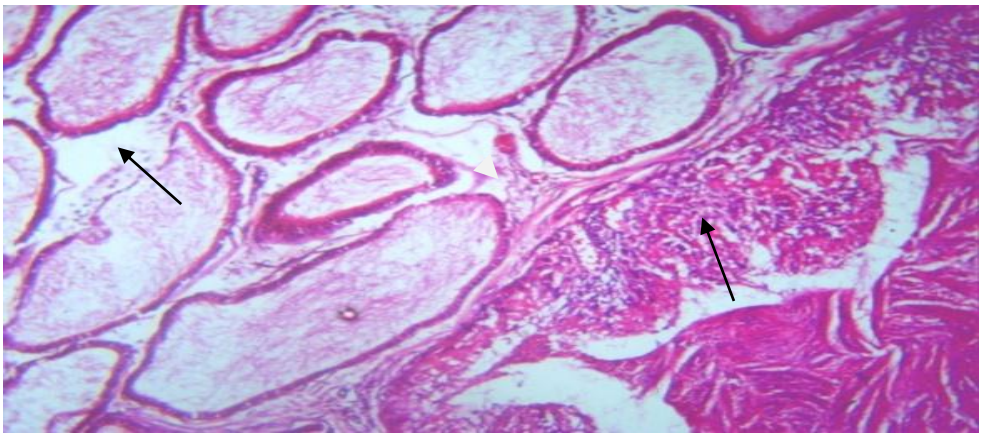


Plate 2 (Group B): showing severe degeneration with severe hyperplasia leading to dilated prostatic gland with mild loss of prostatic secretion corpora amylacca and focal area of severe inflammation

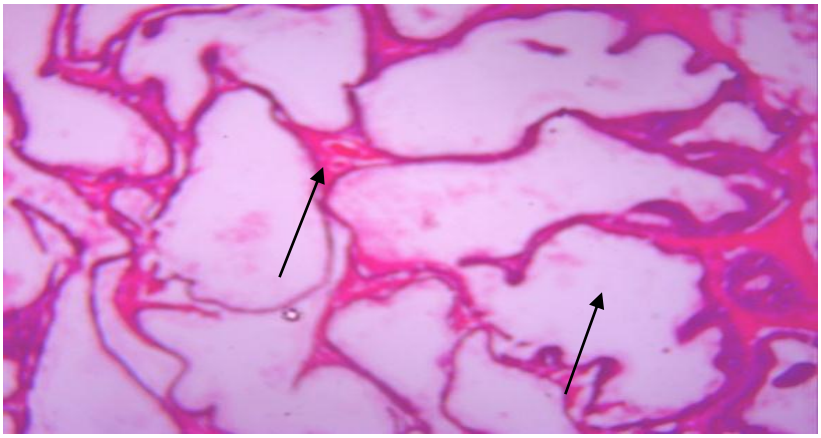
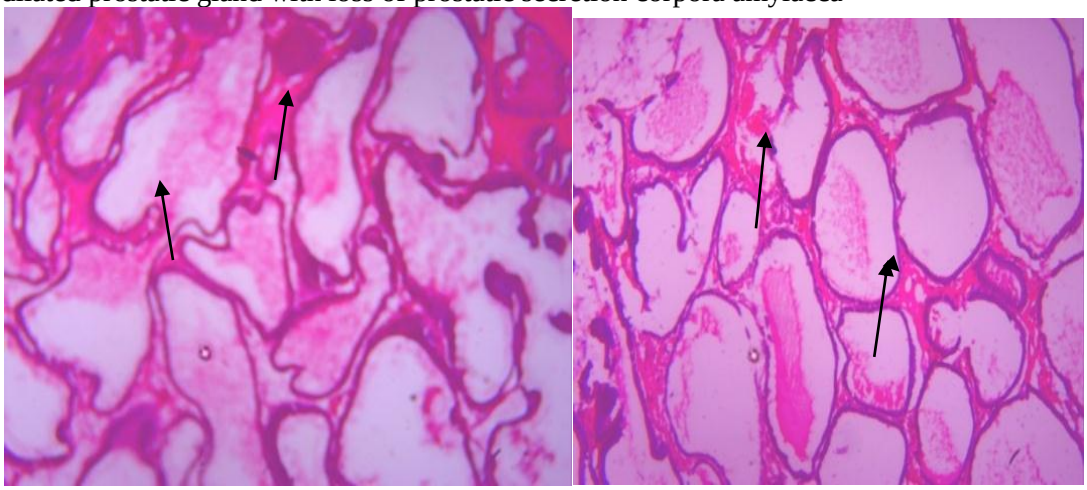
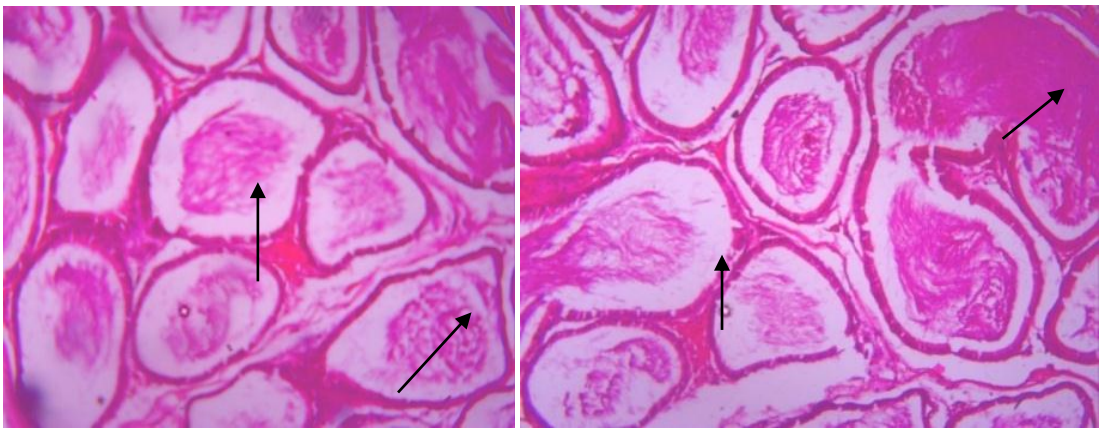


Plate 3 (Group C): showing severe degeneration with severe hyperplasia leading to severe dilated prostatic gland with loss of prostatic secretion corpora amylacca



D_1 D_2



D_3 **D_4**

Plates 4 and 5 (D_1 - D_4): showing different degrees of moderate degenerative hyperplasia leading to mild dilation of the prostatic gland secretion corpora amylacca with focal area of inflammation

Conclusion and Recommendations

Foam-mat dried soursop (*Annona muricata L.*) smoothie powder extract, rich in *annonacin* (an *annonaceous acetogenin*), demonstrated a suppressive effect on epithelial hyperplasia in rats with experimentally induced BPH, as evidenced by lowered PSA levels. However, higher doses resulted in significant changes to renal function parameters, suggesting that excessive consumption could pose nephrotoxic or neuro-degenerative risks. Moderate consumption of soursop products is therefore recommended to balance its potential therapeutic benefits and possible adverse effects.

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