6th International Electronic Conference on Medicinal Chemistry
1-30 November 2020
sciforum.net/conference/ECMC2020
sponsored by pharmaceuticals

Chromolaena odorata ethanol leaves extract attenuated testosterone-induced benign prostatic hyperplasia in male albino rats

Ifeoma Felicia Chukwuma[1]*, Nene Orizu Uchendu[1], John Izuchukwu John[1], and Lawrence Uchenna Sunday Ezeanyika[1]

Presented by: Chukwuma Ifeoma Felicia

[1]*Department of Biochemistry, Faculty of Biological Sciences, University of Nigeria, Nsukka,*

* Corresponding author: chukwuma.ifeoma@unn.edu.ng; *odoifeoma1@gmail.com* .

Abstract

Benign prostatic hyperplasia (BPH), characterized by the proliferation of the stromal, and epithelial cells is one of the most frequent diseases in aging males. This study investigated the effect of ethanol leaves extract of *Chromolaena odorata* on testosterone-induced BPH in male albino rats. BPH was induced by subcutaneous injection of testosterone to experimental groups (B-F) for 28 days. Group A was not induced (normal control, received carboxymethyl cellulose (vehicle), group B (BPH-control) received vehicle while group C received 1 mg/kg body weight of finasteride (standard control), and groups D-F were administered different doses (100, 200, 400 mg/kg body weight) of the extract respectively for 21 days. Blood samples collected from the animals through retro-orbital bleeding after overnight fast were used for determination of prostate biomarkers using standard methods. Results show that Group C, and groups D-F, had reduction in serum levels of testosterone, dihydrotestosterone, prostrate sensitive antigen, malondialdehyde, aspartate aminotransferase and alanine aminotransferase activities, and an increase in superoxide dismutase and catalase activities compared with BPH-control. The results from this study showed that *Chromolaena odorata* leaves extract attenuated testosterone-induced BPH anomalies possibly through the prevention of oxidative stress making it promising phytotherapy for management of BPH in males.

Keywords: Chromolaena *odorata*; oxidative stress; benign prostatic hyperplasia; prostate sensitive antigen; antioxidants activity.

Introduction

➢Benign prostatic hyperplasia (BPH), a non-cancerous proliferation of epithelial, and stromal cells of the prostate gland is one of the most common age related diseases in aging men.

➢Causes of BPH include but are not limited to the following:

- Age.
- Oxidative stress.
- Inflammation.
- Hormones.
- Metabolic syndrome.

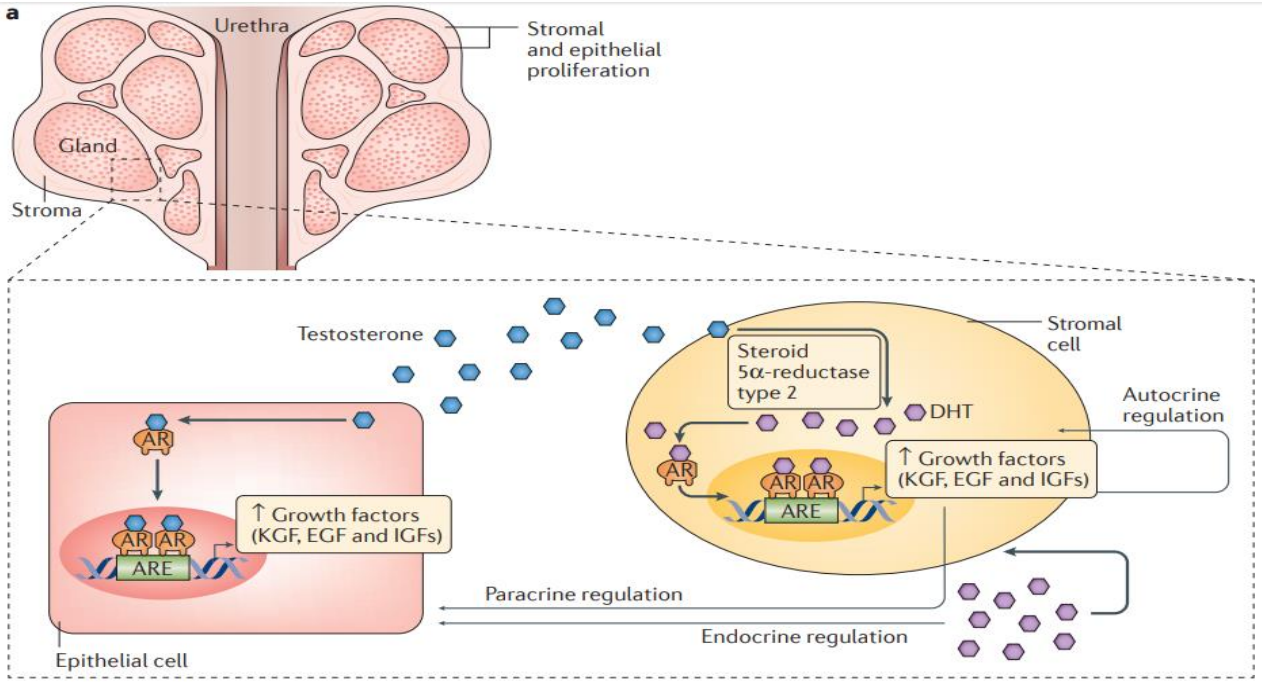

Fig. 1a: Role of testosterone in benign prostatic hyperplasia.

Chughtai *et al*., Nat Rev Dis Primers. 2016, 2:16031.

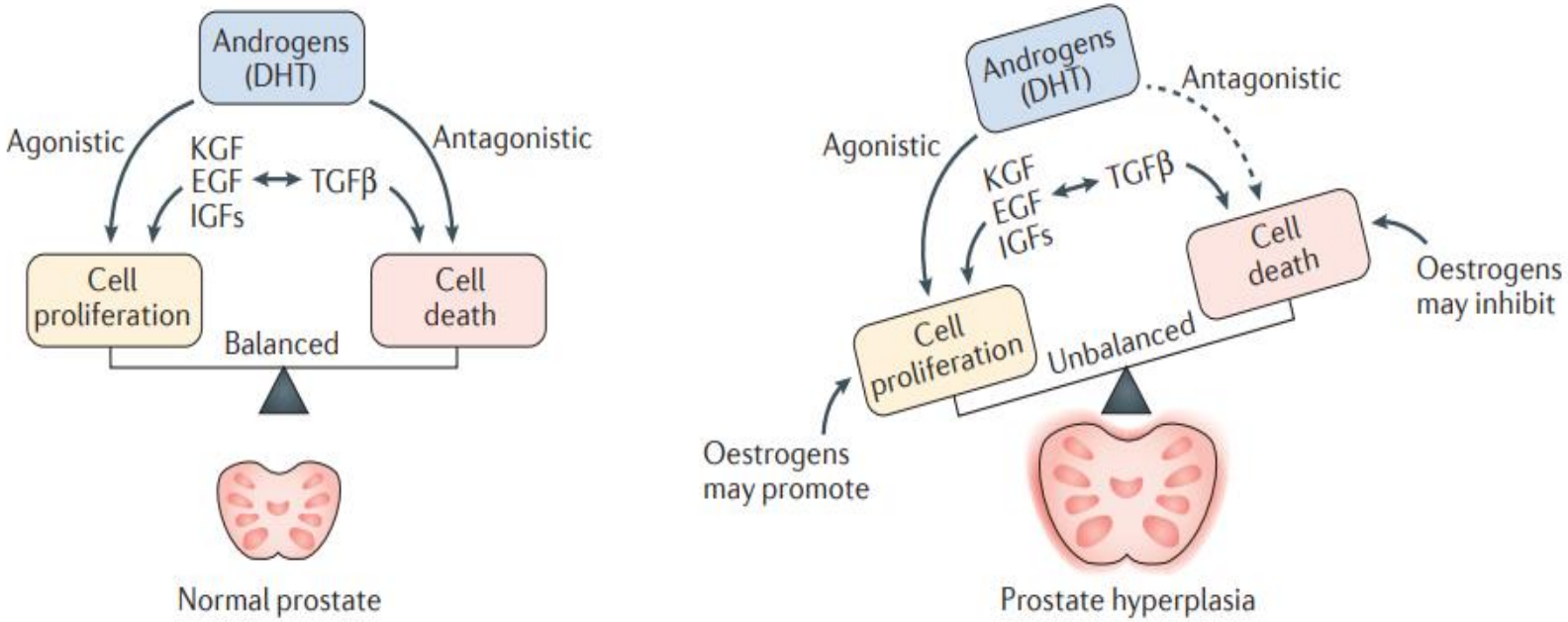

Fig. 1b: Molecular control of prostate growth.

Chughtai *et al.*, Nat Rev Dis Primers. 2016, 2:16031.

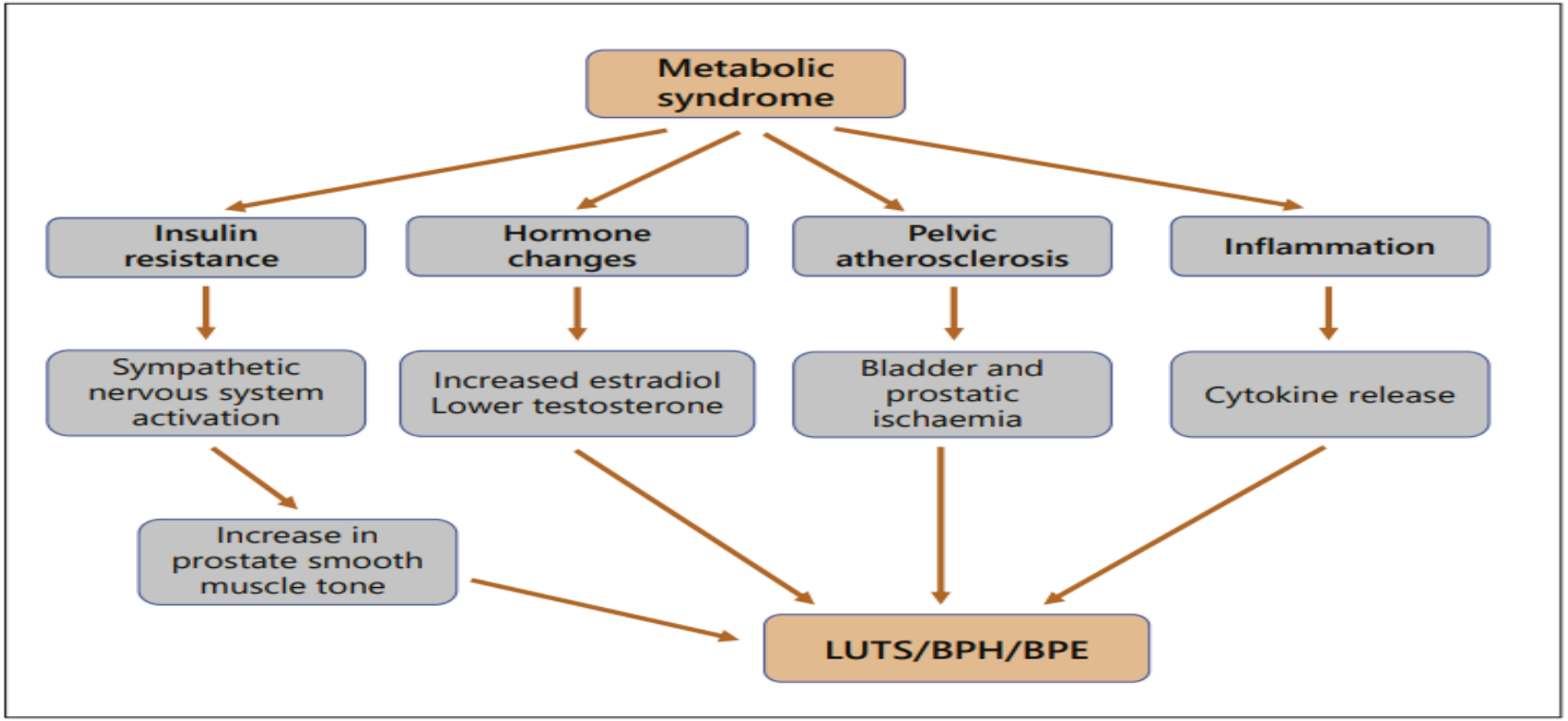

Fig 2. Role of metabolic syndrome in BPH development and prognosis

Madersbacher *et al.*, Gerontology, 2019, 65: 461

➢Symptoms of benign prostatic hyperplasia

- Mild cases of benign prostatic hyperplasia cause obstruction of urine flow, and bladder infection.

- Severe case lead to thickening of bladder due to slight deposition of stone leading to in irreversible bladder damage, kidney failure, sepsis, hepatic failure, and ultimately death (Meludu *et al*. 2017).

Management approaches

- Watchful waiting: This includes advice about life style changes that can ameliorate symptoms (Nyami et al.2016).

- Medical therapy: The most commonly drugs used for BPH are α- blockers, and 5α-reductase inhibitors (Ikeyi *et al*. 2020; Sun *et al*. 2020).

- Surgery : This could be in form of prostate tissue compression, debulking of the adenoma and adenectomy (removal of adenoma) (Chughtai *et al*.2016)

Need for alternative management approach for BPH

- Watchful waiting: Lack of self discipline may worsen symptoms over time.
- Medical therapy: Hypotension, nasal congestion, headache, and sexual dysfunction.
- Surgery: High cost of surgery, urinal tract infection, permanent sexual side effect and urinary incontinence.

Chromolaena odorata also known as Siam weed, bitter bush or Christmas bush is a perennial herb which belongs to Asteraceae family (Vijayaraghavan *et al*. 2017).

Fig. 4: Morphology of *Chlorolaena odorata* leaves
Source: Ifeanyi et al, IOSR-JPBS, 2016, 50.

Pharmacological activities identified in the plant extract(s) include: Antioxidant, anti-inflammatory, anti-diabetic, hemostatic, hepatoprotective, anticancer and immunomodulatory activities (Vijayaraghavan et al 2017; kanase and Shaikh 2018).

Compounds isolated from the plants

Phenolic compounds have been isolated such as p-coumaric, vanillic acids, p-hydrobenzoic acid, and flavonoids such as flavones, chalcones, and flavonols (Kanase and Shaikh 2018).
Flavonone called odoratin (1)

➢Materials and methods

Identification & extraction of *Chromolaena odorata* leaves.

Experimental design

A total of thirty male albino rats divided into six groups of five animals each used for this study were treated as follows:

Group A: Not induced and not treatment, given only vehicle, carboxymethyl cellulose (Normal control)

Group B: BPH-induced and not treatment, given only vehicle (BPH- control)

Group C: BPH- induced and treated with 1 mg/kg b. w of finasteride (Standard control)

Group D: BPH induced and treated with 100 mg/kg b. w of the ethanol extract

Group E: BPH induced and treated with 200 mg/kg b. w of the ethanol extract

Group F: BPH induced and treated with 400 mg/kg b. w of the ethanol extract

Methods

These outlined methods were used in this study:

- Phytochemical screening was done by methods describe by Harbone (1973); Trease and Evans (1989)
- Acute toxicity study was done by method of Lorke (1983).
- Prostate status was investigated with Randox commercial kits.
- Antioxidant status was ascertained using method of Wills (1966; MDA), Fridovich (1989; SOD), Luck (1951, CAT).
- Liver function enzymes activities was determined with Randox kits
- Lipid profile was as investigated with Randox kits

Results and discussion

Table 1: Quantitative Phytochemical constituent of ethanol leaves extract of *Chromolaena odorata*

Phytochemicals	Amount (mg/g)
Tannins	0.72 ± 0.01
Saponins	1.74 ± 0.03
Flavonoids	0.93 ± 0.03
Alkaloids	1.63 ± 0.02
Steroids	0.40 ± 0.01
Glycosides	0.21 ± 0.02

Values are expressed as Mean ± SD, n=3

Table 2:Acute toxicity study (LD_{50}) of ethanol leaves extract of *Chromolaena odorata*

Doses in mg/kg body weight	Number of deaths recorded
Phase 1	
10	0/3
100	0/3
1000	0/3
Phase 2	
1600	0/3
2900	0/3
5000	0/3

n=3

Table 3: Effect of ethanol leaves extract of *Chromolaena odorata* on prostate status of BPH-induced rats

GROUPS	Testosterone (ng/ml)	PSA (ng/ml)	DHT (ng/ml)
A	3.40 ± 1.71 [a]	2.18 ± 0.94 [a]	2.78 ± 0.70 [a,b]
B	8.96 ± 0.77 [d]	6.72 ± 2.13 [c]	3.26 ± 0.69 [b]
C	4.14 ± 0.88 [a, b]	2.90 ± 1.25 [a, b]	2.24 ± 0.20 [a]
D	7.68 ± 1.12 [c,d]	4.30 ± 1.64 [b]	2.74 ± 0.73 [a, b]
E	7.02 ± 2.06 [c,d]	3.56 ± 0.39 [a, b]	2.30 ± 0.21 [a]
F	6.02 ± 2.24 [b,c]	3.22 ± 0.73 [a,b]	2.40 ± 0.46 [a]

Key: Group A: Not induced and not treatment (Normal control; given carboxymethyl cellulose (vehicle)), Group B: BPH induced and not treatment, given only vehicle (BPH- control), Group C: BPH induced and treated with 1 mg/kg b. w of finasteride (Standard control) and Groups D-F: BPH induced and treated with 100, 200 and 400 mg/kg b. w of the ethanol extract respectively.

Table 4: Effect of ethanol leaves extract of *Chromolaena odorata* on malondialdehyde level, and antioxidant enzymes of BPH-induced rats

GROUPS	MDA (mg/ml)	SOD (U/mg)	CAT (U/mg)
A	1.56 ± 0.52 ^{b}	11.12 ± 0.17 ^{b}	2.50 ± 0.23^{a,b}
B	2.64 ± 0.61 ^{c}	10.76 ± 0.21 ^{a}	2.05 ± 0.18 ^{a}
C	0.91 ± 0.22 ^{a}	10.92 ± 0.31 $^{a, b}$	3.35 ± 0.54 ^{a,b,c}
D	2.78 ± 0.28 ^{c}	10.92 ± 0.13 $^{a, b}$	3.21 ± 0.25 $^{b, c}$
E	1.46 ± 0.35 $^{a, b}$	11.06 ± 0.15 ^{b}	4.00 ± 0.64 $^{c, d}$
F	1.25 ± 0.45 $^{a, b}$	11.10 ± 0.15 ^{b}	4.20 ± 1.33 ^{d}

Key: Group A: Not induced and not treatment (Normal control; given carboxymethyl cellulose (vehicle)), Group B: BPH induced and not treatment, given only vehicle (BPH- control), Group C: BPH induced and treated with 1 mg/kg b. w of finasteride (Standard control) and Groups D-F: BPH induced and treated with 100, 200 and 400 mg/kg b. w of the ethanol extract respectively.

Table 5: Effect of ethanol leaves extract of *Chromolaena odorata* on liver function enzymes in Testosterone-Induced Rats

GROUPS	AST (IU/L)	ALT (IU/L)
A	19.80 ± 2.04 [a, b]	19.20 ± 7.39 [a,b]
B	23.40 ± 4.03 [b]	30.80 ± 7.82 [c]
C	17.80 ± 2.86 [a]	15.60 ± 4.82 [a]
D	20.60 ± 2.19 [a,b]	30.20 ± 4.38 [c]
E	18.80 ± 2.38 [a]	25.00 ± 6.44 [b,c]
F	18.20 ± 2.68 [a]	20.60 ± 6.87 [a,b]

Key: Group A: Not induced and not treatment (Normal control; given carboxymethyl cellulose (vehicle)), Group B: BPH induced and not treatment, given only vehicle (BPH- control), Group C: BPH induced and treated with 1 mg/kg b. w of finasteride (Standard control) and Groups D-F: BPH induced and treated with 100, 200 and 400 mg/kg b. w of the ethanol extract respectively.

Table 6: Effect of ethanol extract of *Chromolaena odorata* on lipid profile of BPH-induced rats

GROUPS	CHOL (mmol/L)	TAG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)
A	4.74 ± 1.76 ^{a}	1.82 ± 0.20 ^{a,b}	5.04 ± 0.39 ^{a,b,c}	1.48 ± 0.41 ^{a}
B	7.82 ± 1.36 ^{b}	2.29 ± 0.42 ^{c}	3.88 ± 1.18 ^{a}	2.32 ± 0.52 ^{b}
C	4.57 ± 0.65 ^{a}	1.66 ± 0.31 ^{a}	5.60 ± 0.48 ^{b,c}	1.04 ± 0.26 ^{a}
D	7.62 ± 1.67 ^{b}	2.22 ± 0.29 ^{b,c}	4.63 ± 0.34 ^{a,b}	2.22 ± 0.34 ^{b}
E	7.27 ± 1.09 ^{b}	2.15 ± 0.31 ^{b,c}	5.15 ± 1.18 ^{b,c}	1.50 ± 0.39 ^{a}
F	5.32 ± 1.23 ^{a}	1.92 ± 0.24 ^{a,b,c}	5.98 ± 1.03 ^{c}	1.32 ± 0.71 ^{a}

Key: Group A: Not induced and not treatment (Normal control; given carboxymethyl cellulose (vehicle)), Group B: BPH induced and not treatment, given only vehicle (BPH- control), Group C: BPH induced and treated with 1 mg/kg b. w of finasteride (Standard control) and Groups D-F: BPH induced and treated with 100, 200 and 400 mg/kg b. w of the ethanol extract respectively.

Conclusions

Results from this study showed that leaves extract of *Chromolaena odorata* reduced levels of testosterone, PSA, DHT, liver enzymes activities as well as cholesterol, triacylglycerol, and LDL-C, and increased antioxidant enzymes activities compared with the BPH-control. These findings indicates that leaves extract of *Chromolaena odorata* attenuated BPH anomalies and could be employed as promising phytotherapy for BPH treatment. However, the exert molecular mechanisms of its action needs to be ascertained.

Acknowledgments

The authors want to appreciate all the post graduate students, technical staff, and lecturers of the Department of Biochemistry, University of Nigeria, Nsukka, Nigeria who contributed towards the success of this research work

THANK YOU FOR LISTENING