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Hematological, biochemical and bacteriological assessment after phytotherapy of benign prostate hyperplasia using *plantago major* and *solanum aculeastrum* in Goma

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Abstract
Phytotherapy can be integrated in medical treatment for benign prostatic hyperplasia at the same level as alpha blockers, and 5-alpha-reductase inhibitors.
The objective of this study was to investigate the toxicity of local plants used by traditional medicine, namely *Plantago major* and *Solanum aculeastrum* in comparison with an alpha Blocker (Alfuzosin 10 mg).
Male patients aged 60 and above were randomly assigned to two groups. Each group contained of 68 patients who had been diagnosed with prostate cancer based on pathology. One group was given the phytotherapy and the other Alfuzosin. The study was conducted over a period of 27 months from 1st January 2019 to 31st March 2021. The phyto-medication was given for 3 months followed by 6 months break, with a total of 3 episodes. Alfuzosin was administered at dosage of 10 mg tablet per day.
Haematological, biochemical and urinary bacteriological tests were done at the beginning of the study, after each episode and at the end. The initial results were compared with the final results after treatment. Results were entered by the SPSS statistcs software version 23 and the χ^2 test was used for significance.
The haematological and urinary bacteriological tests did not undergo any modification in the two groups whereas a significant improvement occurred in the biochemical tests on the kidney, the liver and the metabolism in favor of herbal medicine.
The conclusion was that phytotherapy of benign prostatic hyperplasia is not harmful. It is appropriate, and acceptable to patients who adhere to the treatment. Further studies could assess the pharmacokinetic aspects to establish the relationship between the pharmacochemical compounds of these plants with the prostate tissue. This also raises the possibility of developing a phyto-drug.

Keywords: Phytotherapy, *Plantago major*, *Solanum aculeastrum*, biochemical improvement

Introduction
Herbal medicine is both an ancestral and modern science which consists in "healing by plants" [1, 2]. It is currently part of the medical treatment which managed voiding disorders alongside α1 blockers and anti 5α reductases [3, 4]. Medical treatment has replaced conventional treatment, such as surgery alone [4]. It aims to relieve symptoms, delay disease progression and avoid surgical treatment [1, 2, 5, 6,7].
The WHO has accepted the Florida dwarf palm (Serenoa repens ou Saw palmeto Permixon®), ®), African plum (Pygeum africanum Tadenam®) etc. as a model of herbal medicine in benign prostatic hyperplasia (BPH) [8, 9, 10, 11, 12, 13].
However, the choice of phytomedicine depends on the authors as well as on the geographical location. Therefore So in India, recourse is made on Himplasia (a polyherbal medicine made from terrestrial Tribulus, Cadsalpina bonducella, Crataeva nurtala, Areva catechu, Aspertagus racemosus and Akita pichti) all of which have antibiotic and anti-inflammatory properties, diuretics and which had a proven action as α1 blockers and anti 5α reductases [14, 15].
In Vietnam, Crinum latifolium has been reported by authors from that country [16]. Chinese authors have claimed that herbal remedies perform better than Western drugs with evidence from randomized and comparative studies [17]. In Nigeria Olapade O E *et al*. reported good results with Lycopersicum esculenta (Cocos nucigera) in the treatment of BPH [18] while

Usunabun U et al. used the leaves of Annonay muricata [19]. Also in Nigeria Abdullani recourses to Serenoa repens was adapted under the label of Prostacare® at Aminu Kano Teaching Hospital (AKTH) and prescribed with good results [20].

In 2019 in Goma, we conducted a trial study on the use of herbal medicine for voiding disorders in males aged 50 or above using traditional medicine by prescribing Plantago major and Solanum aculeastrum. This indication was not yet recognized in the literature. The preliminary results, after a first episode of treatment of 3 months over a planned course of 27 months were satisfactory. Indeed, this treatment improved the International Prostatic Symptoms Score (IPSS) and the quality of life (QoL) score of 36 patients by transforming cases with a severe score to a mild score within this treatment time [21]. Plantago major of the Plantaginaceae family and Solanum aculeastrum, a Solanaceae, are two plants recognized at the Lwiro National Herbarium, the first registered at No. 2193 by Christiansen AR on March 20, 1958, the second at No. 2993 by Troipin G on January 20, 1957 [22].

The chemical content of these plants is polysaccharides and polyphenols, more precisely glycosides, iridoides, flavonoids, tannins, phenylethanoids, alkaloids which have various therapeutic properties: anti-inflammatory, anti-ulcer, antioxidant, antiviral, anticancer [23, 24]. They are therefore useful in the treatment of several pathologies including depression, hypertension, chronic wounds, traumatic inflammation of the liver, respiratory diseases, diet, etc. [23, 24, 25]. We recognized during the previous study their effectiveness on IPSS [21].

However the possible toxicity of this herbal medicine was unknown.

To answer this question, we conducted a new clinical trial on two groups of patients, one subjected to modern treatment with Alfuzosin and the other to herbal medicine, with the aim of demonstrating the safety of herbal medicine at Plantago major and Solanum aculeastrum from hematological, biochemical (kidney, liver, metabolism) and bacteriological tests.

Material and Methods

Our study consisted of a clinical trial on two cohorts of patients recruited according to the principle of Durand C [26] and distributed randomly, so that 68, were prescribed with the phyto-medication, the dosage of which is described in the previous study entitled "Phytotherapy voiding disorders in males aged 50 or over in Goma " [21] and 68 with Alfuzosin 10 mg tablet, at a dosage of 10 mg per day. All patients were at least 60 years old with moderate and or severe but uncomplicated IPSS and no decompensated comorbidities.

-The histopathological examination had previously confirmed the diagnosis on echo-guided biopsy specimens using the sampling needle mounted on an endorectal probe on the Bruel and Kjaer Medical (BK Médical) 7.5MHZ (USA 2005) ultrasound machine by the Medical imaging specialist.

-The histopathological examination was carried out by the doctor specializing in histopathology.

The duration of the study was 27 months divided into 3 episodes of 9 months each. Herbal medicine was administered for 3 months followed by a 6 months break corresponding to an episode while Alfuzosin was administered daily as one 10mg tablet.

The analyzes were made

1. Haematological tests

- Full blood count using the CYANhemato machine (China 2010) for hemoglobin, hematocrit, white blood cells, leukocyte formula, red blood cells, reticulocytes and platelets.
- Bleeding profile: the prothrombin level and prothrombin time by the Vidas machine (bioMérieux Australia put into service in 2021 (normal level> 70% and 11-13 seconds respectively).
- The bleeding time (Ts) by the Ivy technique (normal time 2-6 minutes) and the clotting time (Tc) by the Duke technique (normal time 2-5 minutes).

2. The biochemistry tests were carried out using the Genrui automaton (Model GS 200 China 2019). It was about for:

- **Kidney:** the blood level of creatinine (normal: 0.9-1.1 mg / dl man, 0.7-1 mg / dl woman) and urea (normal: 18-45 mg / dl man, 15 -42mg female),
- **Liver:** the level of alanine aminotransferases (ALAT) (normal: 8-35 International Units / liter (IU / L)) and aspartate-aminotransferases (ASAT) (normal: 8-35 IU / L),
- **Metabolic tests:**
- Uric Acid Blood Level (Normal: 4-7mg / Dl)
- The Blood Cholesterol Level (Normal: <200 Mg / Dl)
- The Fasting Blood Sugar Level Was Measured Using The Code Free Strips (Blood Glucose Monitoring Sd Bionsensor, Inc Korea 2021), Normal Level: 70-110mg / Dl On An Empty Stomach, <140 Mg / After Meal.

3. The ECBU was made on a microscope (Olympus Belgium 2019) after centrifugation (centrifuge Model 80-26.CAP.20mlx12) for the Gram, the culture on Petri dishes (Belgium 2016) was indicated in case of positivity. The antibiogram was done in the latter case.

Samples were taken from each patient in each group of 68 persons at the start of the study, after each episode of 9 months and at the end of the study, for a total of 4 tests. The results We present the results of the beginning and those of the end of the study; from January 1st, 2019 to March 31, 2021 for concision. Data processing and analysis were performed using SPSS version 23 software and significance level by χ^2 p 0.05.

The results have been presented in the form of histograms with legend in the figure.

The rules of medical ethics have been observed: the work has obtained the prior approval of the ethics commission of the faculty of medicine of UNILU (reference CEM UNILU No Approval: UNILU / CEM / 121/2018 of 06 November 2018) and all patients were consenting and well informed about the risk and benefit of the study.

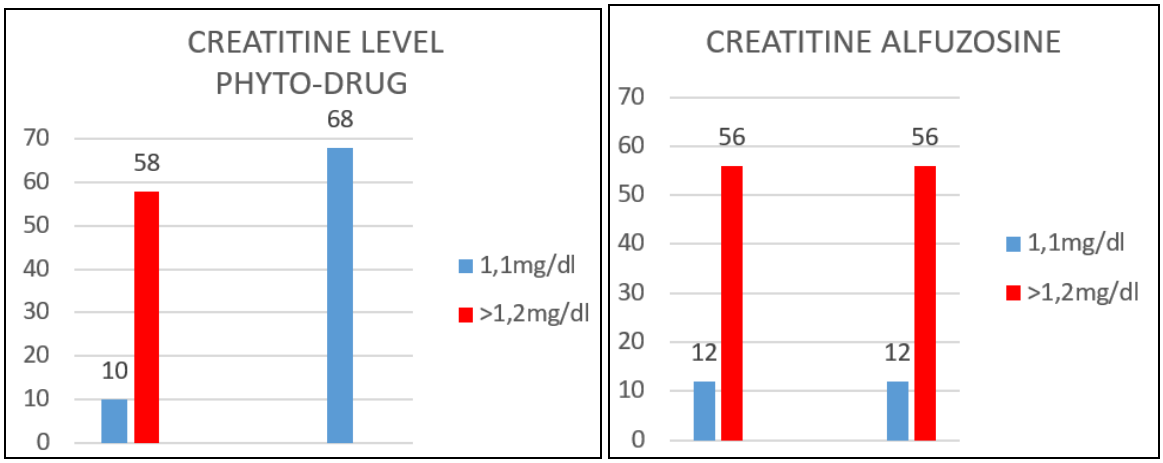
The results were presented as histograms with legend in the figure. We ourselves determined the sub-normal rates and the frankly pathological cases.

Results

1. Haematological Assessment

In the two groups studied, no haematological disturbance was noted for all the parameters studied. In fact, no component of the blood count or any disturbance of coagulation was noted in the two series.

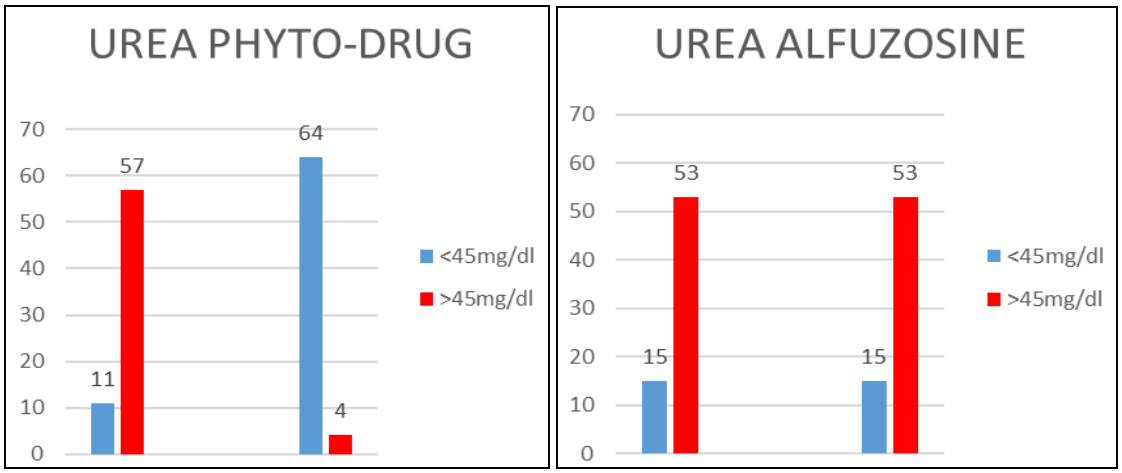
2. Biochemistry Assessment
° Renal assessment
Serum creatinine



Graph 1: Blood creatinine level

During the phyto-medication, the pathological levels (> 1.2mg) normalized from 10 to 60 cases, so that a significant improvement compared to the Alfuzosin group where no change was not noted (P-value for chi-square test of 0.000< 0.05).

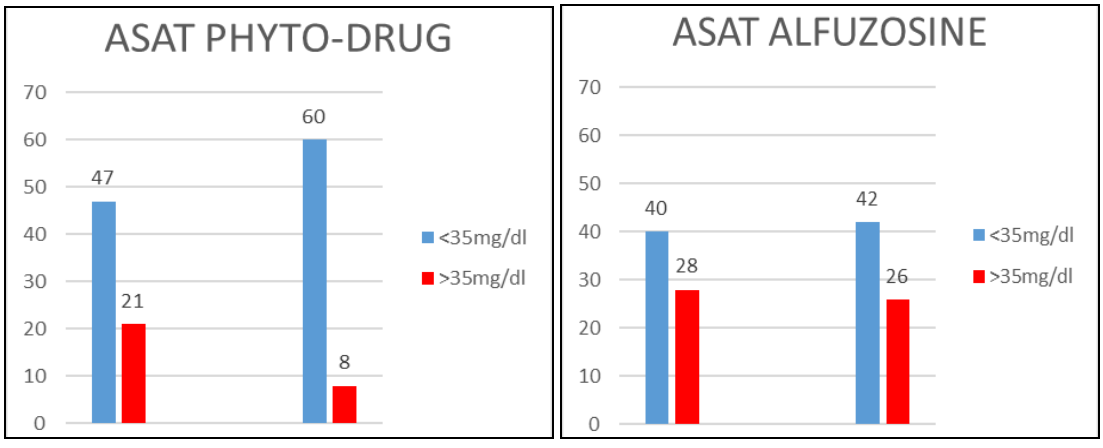
Blood urea level



Graph 2: Blood urea level

In the herbal medicine group, urea blood levels are normalized in 64 patients compared to 11 at baseline, that is a positive linear progression with an improvement of more than 100% (chi-square=72.578 with P-value of 0.000 > 0.05).

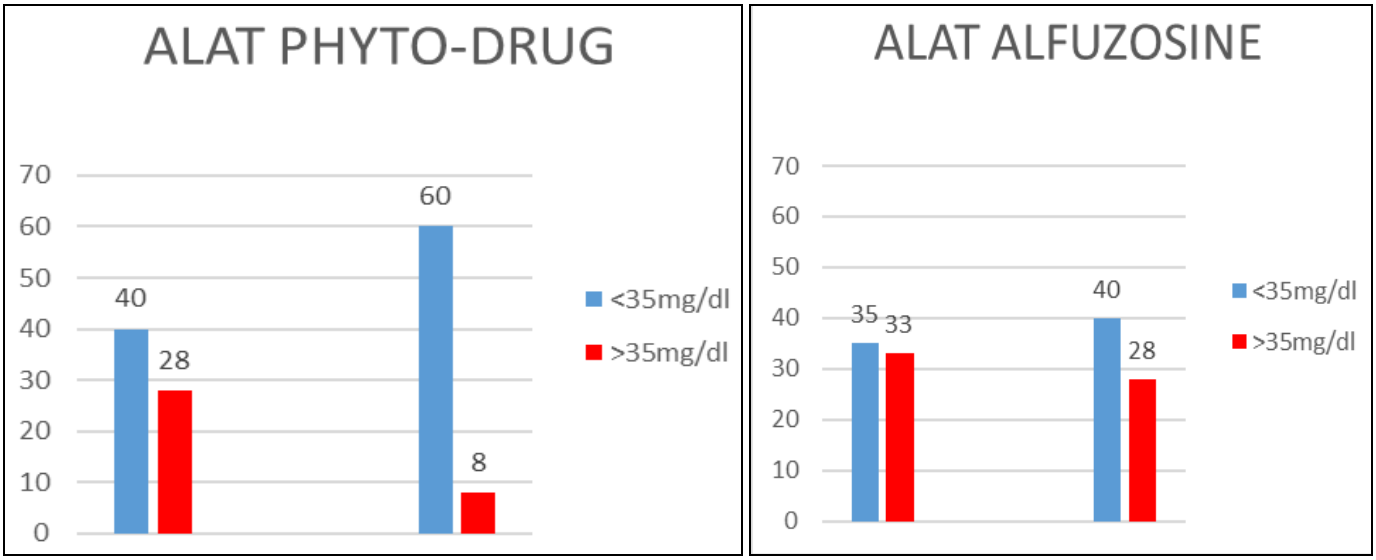
° Liver test
AST



Graph 3: AST liver test

The liver function test (AST) was not negatively disturbed in the two groups but improved slightly in the first group. Indeed, the normal rates of AST concerned 60 patients at the end compared to 47 at the beginning, that is to say a linear progression of an improvement of 27% (chi-square =11.578 with P-value of 0.03<0.05).

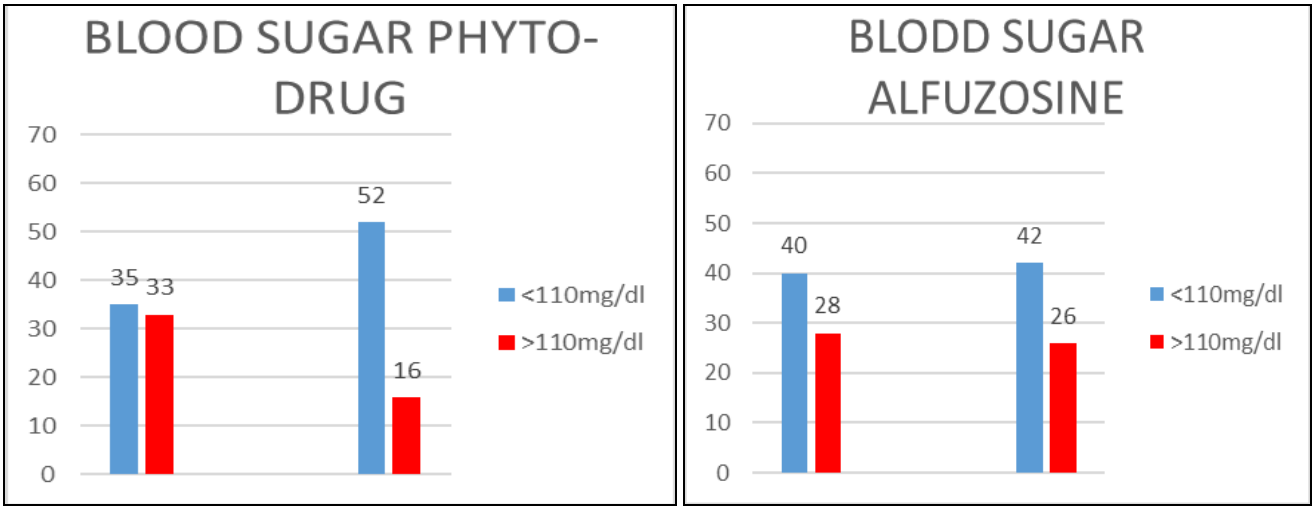
ALT



Graph 4: ALT liver test

ALT levels improved after phyto-medication than with alfuzosin (50% vs. 14.2%) (chi-square of 15.111 with P-value of 0.000 < 0.05).

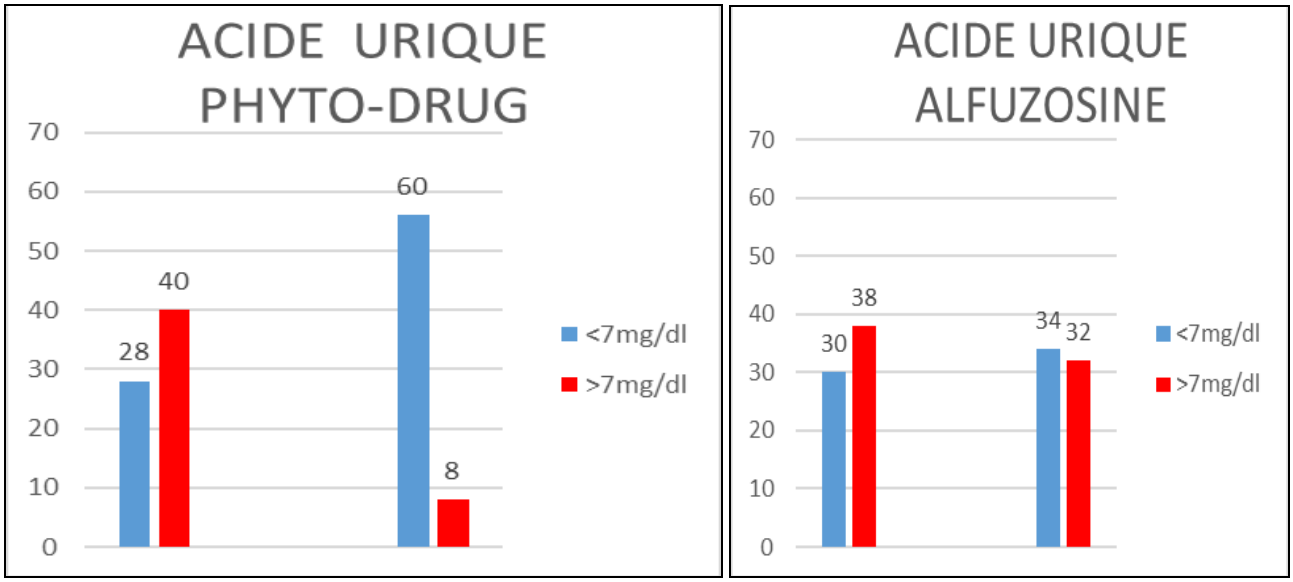
Blood sugar



Graph 5: Blood sugar level

The number of cases with improved fasting glycemia was superior in the phyto-drug group than in that of Alfuzosin, that is 48.5% against 6% (Chi-square of 3.980 with P-value of 0.137>0.005).

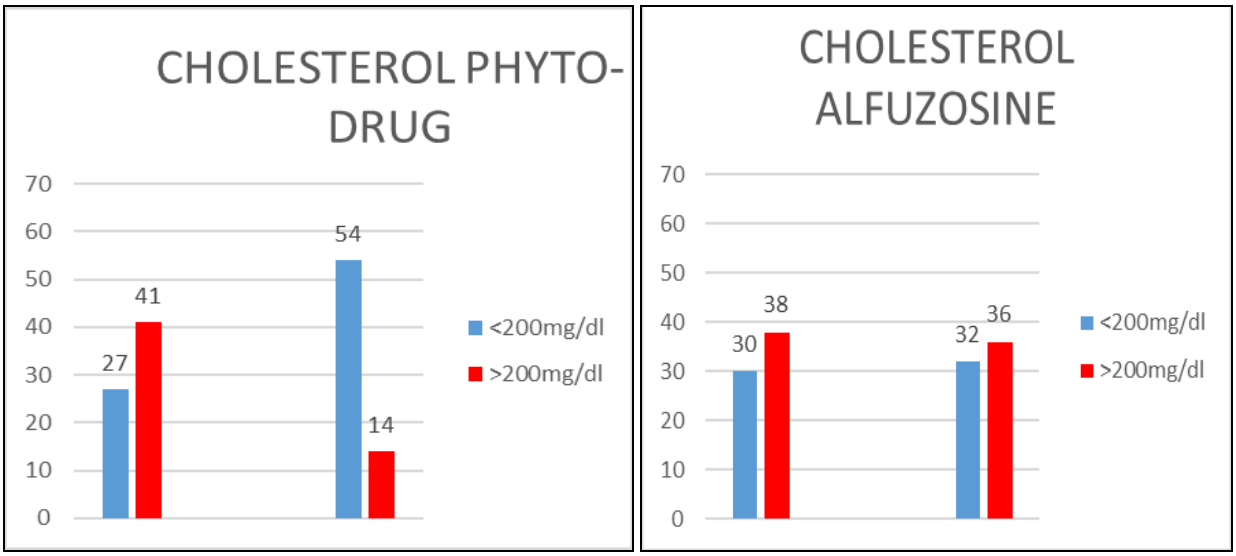
° Metabolic balance
Blood uric acid level



Graph 6: Blood uric acid level

Better normalization of uric acid in the phyto-drug group: 28 to 56 cases.
For the phyto-drug the improvement is over 100% in term of the number of patients on the biginning, while for Alfuzosin it is 13.3% (Chi-square test of 17.990 with P-value of 0.000<0.05).

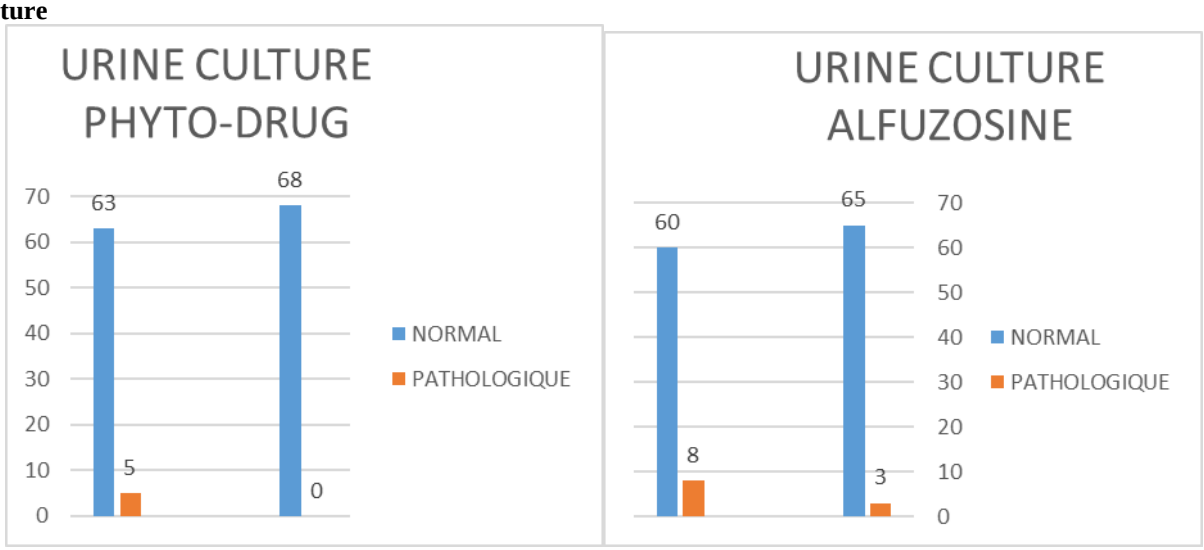
Blood cholesterol level



Graph 7: Blood cholesterol level

The cholesterolemia improved with the phyto-drug treatment at 100%, therefore better than that of ALFUZOSINE which is 6%. The hypercholesterolemia disappeared in the herbal medicine group (Chi-square test of 19.730 with P-value of 0.000<0.05).

8. Bacteriology Result
Urine Culture



Graph 8: Urine Culture pre and post processing

In both groups, URINE CULTURE results remained for most of the patients normal. The difference observed was not significant between the two groups (Chi-square of 3.980 with P-value of 0.137>0.005).

Discussion

Acute toxicity was defined by Rasolofonanteia RR in his thesis on the phytochemical and biological study of extracts from the leaves of Astrotrichilia parvifolia (Meliaceae), a Madagascan medicinal plant, as an effect that occurs immediately or the first days after exposure [27].

In this case the liver and kidneys are the target organs because they are vulnerable and more exposed to toxins than other irrigated or less active organs or tissues such as skin and bones.

Hajjaj Gh in Morocco said that the chronic toxicity also concerns the spleen [28]. Even if the authors of all the non-toxic character of herbal medicine in general Aboyade O *et al*. (South Africa) have reported the interest of controlling weight, hematology and biochemistry in the monitoring in particular of herbal medicine Solanum aculeastrum [29].

These recommendations were followed for our plants except for weight and have added urine cyto-bacteriology for our plants. At the end of our study, no acute or chronic toxicity was identified, neither clinically (in accordance with the results of one of our previous studies) [21] or by laboratory workup.

Blood level of creatinine and urea

Our study showed that during the phyto-drug, the subnormal levels of creatinine (1.2-2 mg / dl) and the pathological levels (> 2 mg) normalized from 10 to 60 cases, so that an improvement of more than 100% different at Alfuzocine where no change was noted.

Urea levels are normalized in 64 patients compared to 11 at baseline, which is also an improvement of more than 100%.

Rasolofonanteia located the kidney damage in the glomeruli and convoluted tubes resulting in kidney failure. He classified these intoxications as acute (delay ≤ 24 hours in a single attack), subacute (1 month), subchronic (1-3 months) and chronic (> 3 months) and as repetitive attacks for the last three categories [27].

Barney R [30] recommended the dosage of creatinine and urea as well as the PSA before the rectal examination so that they may not disturb the results by the massage of the prostate.

Koné A reported that creatinine results from the breakdown of creatine, an essential protein of muscle masses and is excreted by the kidney. As such, it is an indicator of muscle mass and renal function [31]. Urea is an end product of the metabolism of purines, the essential protein in muscle, and as such is a good indicator of catabolism and renal failure [31]. The dosage of these two tests is done concomitantly.

We noticed, at the end of our study that the phyto-drug had a beneficial and not a toxic effect on the kidneys.

Blood levels of ALT and AST

In our series, the ALT levels improved more after the phyto-drug than with alfuzosin (50% vs. 14.2%). The normal AST levels concerned 60 patients at the end compared to 47cases at the beginning, that is a linear progression of an improvement of 27%.

For Koné A, the ALT and AST transaminases are the most important enzymes in the body. They use at the cell level in many chemical processes taking place at the hepatic level [31]. Kien F gave their name synonymous with glutamino-pyruvate-transaminases (GPT) for ALAT and glutamino-oxaloacetate transaminases (GOT) for AST and that they play a very important role in chemical reactions in the liver [32]. She also said that their ratio is not always equal, so if the ALT / AST ratio is <1 this is related to mild hepatitis while> 1 is equivalent to chronic hepatitis [32]. They are also unevenly distributed in the body more other than the liver. Thus Joaquim C reported the presence of AST in the heart, muscles and skin, while ALTs are mainly in the liver and therefore more specific for hepatic lesions [33]. Transaminases are used to investigate infectious and toxic hepatitis, obstructive hepato-cellular and pancreatic lesions of the bile ducts, hepatic poisoning by alcohol and drugs [33]. The Scientific Council of the Domain of Health in France has determined a few etiologies of hepatic intoxication and hence the elevation of transaminases: alcohol first, exposure to hepatotoxic substances (drugs, food supplements, herbal medicine, illicit substances and other toxins) [34]. The Council also noted that the syndrome constituting a risk factor. They reported the normal and pathological values of transaminases in five stages (Dynamed 2019):

1. Normal < twice the normal value,
2. Very moderate: 2 to 5 times the normal value,
3. Moderate: 5-15 times the normal value,
4. Severe: > 15 times the normal value,

5. Major: > 10000IU / l.

For Decock C, if the liver is disrupted the transaminases infiltrate the blood and their concentration rises up, signifying cell destruction [35]. However, Reynier C in his thesis on low disturbance of transaminases in general medicine asserted that their tests are specific but not sensitive. They do not have a direct correlation between their elevation and the degree of hepatic necrosis [36]. That is to say, they remain, at the very least, orientative and not pathognomonic. In the recommendations of the Primary Medicine Service of the University Hospital of Geneva (DMCPRU-HUG) it appeared that the risk factors consistent with exposure to any hepatotoxic substance. In the event of chronic liver disease, the only syndrome contracted and only having a rate of ALT> twice the normal value for a month or, urgently, before a rate > 5 times the normal [37] should be treated.
From what precedes, our study finds its justification here. It showed that the phyto-drug with our plants was very far from being toxic to the liver but that it would even be a good hepato-protector.

Uric acid
We observed in our study a normalization of the blood uric acid level better with the phyto-drug group: 28 to 56 cases. Thus the improvement was 100% while for Alfuzosin it was 13.3%.
Justine Pillon, 2019 [38] spoke about the factors favoring the precipitation of uric acid due to advanced age:

- 20% of calculations concern the 50-55 age group while 40% concerned subjects over 70 years old.
- Age decreases the power of neutralizing acid charges which increase precipitation.
- It lowers the renal capacity to alkalinize the urine by ammoniogenesis allowing the elimination of endogenous acid loads.
- It promotes urinary stasis favorable to crystallization.

In summary, age is a predictor of uricemia.
Sadenne S added that a physiological product can become pathogenic, namely uric acid. Indeed it is reabsorbed by the kidneys in humans because of the loss of hepatic activity to synthesize urate oxidase (or uricase) which transforms, in other animal species, uric acid into allantoin which, it is then excreted. Or Uric acid and urate are in the plasma in an almost insoluble state ready to precipitate. And yet uric acid is an antioxidant that can prevent cancer. Hence the difficulty of evaluating the benefit / risk between a positive rate for health and a rate that may be pathological [39].
Our study provided reassurance of the beneficial effect of plants on the renal elimination of uric acid in patients in this series. We noted in fact that their age was not a risk factor and that the phyto-medication, as for the parameters which preceded a beneficial role on the renal function.

Cholesterol
Cholesterolemia improved with the phyto-medication to 100%, better than with the Alfuzosin treatment which was 6%. Tanwi Priya identified cholesterol as a lipid that has multiple functions in the human. From its metabolism are derived bile salts, steroid hormones and oxysterols which participate in different biological functions. High cholesterol is an important risk factor for cardiovascular disease, development of atheromatosis, diabetes and Alzheimer's disease. Traditional plants act on cholesterol through the balance between free radicals and antioxidants [40]. Voisin M is his thesis on the metabolism of cholesterol in which cholesterol is an important component of cell membranes and contributes to their rigidity and ordering [41]. Akram Akhtar in his dissertation on the management of hypercholesterolemia in the prevention of cardiovascular disease said that cholesterol is a membrane lipid naturally produced by the body and is essential for life. It is in the blood in esterified form transported by lipoproteins in two ways: low density lipoproteins (low density LDL lipoproteins) which is bad cholesterol which predisposes to cardiovascular disease and high density lipoproteins (high density HDL lipoproteins) which transports cholesterol to the liver to produce its derivatives.
The first is susceptible to oxidation and is the source of harmful free radicals [42].
Zubair Maqsood in his thesis confirmed the harmfulness of the LDL form which predisposes to atheromatosis. The metabolism of the HDL form is controlled by 7-α-hydroxylase which leads to bile salts, their absorption and their enterohepatic cycle [43]. Ninaemeka M discusses the poorly explained relationship of BPH and the illustrious syndrome of which LDL and cholesterol are increased while HDL is lowered [44].
In our study, there is no suggestion that the phytomedication is in any no way harmful to the liver and the metabolism in general, the reflection of which is the blood cholesterol level.

Blood sugar
The number of cases with elevation of the value blood sugar was higher in the phyto-medication group than in that of Alfuzosin, that is 48.5% against 6%. Our findings join Asteer who with the pumpkin improved the diabetes induced in rats by Alloxan [45]. For Koné A, blood sugar responds to age: after 65 years 10% of men are diabetic, 20% after 80 years and 10% have glucose intolerance, insulin resistance and the appearance of abdominal adipose tissue [31]. Alioune C recommended, in Guinea, the control of glycemia by glycated hemoglobin (HbA1C) which guarantees the evaluation of the glycemia over a long period (approximately 2 to 3 months) and by there, to know a little better the history of the disease. [46]. Noémie Hatich described the type 2 diabetes framework that is often discussed in the elderly. In addition to hyperglycemia and insulin resistance, it includes obesity, high blood pressure, dyslipemia. He emphasizes the role of inflammation induced by oxidative stress that will lead to insulin resistance. Over time, the lack of insulin secretion by the pancreas may develop [47]. Gerald Kojiro Thomas also spoke of oxidative stress by excess of free radicals which attack all tissues: the destruction of proteins leads to atheromatosis, the destruction of lipids concerning cell membranes and that of carbohydrates cataracts. He added that in diabetics the level of lipoperoxide was significantly higher than in controls. It was even higher in case of microangiopathies and it was necessary to prescribe antioxidants for prevention [48]. One of the most frequent consequences of these microangiopathies is diabetic foot, the stages of which and the prevention strategy have been dictated by the Directorate for the Fight against Diabetes in the guidelines in the DRC [49]. Mubenga at the provincial hospital of Bukavu cited, among the risk factors for cohabitation of diabetes and BPH, ethnicity in South Kivu and that this fact must be well mastered in the management of patients [50]. From all of the above, despite the age of our patients, we can advance the idea that the phyto-drug has helped to balance, thereby preventing many of its complications.

Urine Culture
Urinary tract infection is, along with acute urinary infection,

hematuria and lithiasis, one of the major complications of BPH able of compromising the initiative of management. It can manifest as prostatitis, cystitis, and / or pyelonephritis. It is diagnosed by Urine Culture and ultrasound [51, 52, 53]. Other authors including ANAES have confirmed that Urine Culture is useful in checking urine sterility [54, 55, 30] and therefore ruling out urinary tract infection [56]. Duperron C quoted it among the elements of the 1st stage of the examination of the patient [57]. In our study, even if the urinary tract infection only concerned a population representing little 8/68 or 12% at the commencement against 3/68 or 4.5% at the end in the Alfusosine series and 5/68 or 7.3% against 0 cases in the phyto-drug series, it remains true that this variable must be taken into account. In fact, a complication of infection is always, in surgery, a major cause of morti-morbidity. In both study groups in our series, Urine Culture results are formed normally for most patients. The difference observed was not significant between the two groups (p: 0.08).

Conclusion

Our 27-month study of BPH treatment with local herbal medicine with *Plantago major* and *Solanum aculeasrtrum* showed the safety of the plants used in Goma without any acute or chronic toxicity compared to conventional treatment. As such, we recommend phytotherapy with *Plantago major* and *Solanum aculeastrum* in the management of benign prostatic hyperplasia and wish to further study the pharmacokinetics and pharmacodynamics of these plants. A dosage form could be encouraged which would even lead to the production of a modern phyto-drug.

What this study adds

The use of *Plantago major* and *Solanum aculeastrum* in the management of benign prostatic hyperplasia is safe.

These plants are used in herbal medicine for benign prostatic hyperplasia in traditional medicine from Goma. Indeed, WHO has recognized herbal medicine and according to geography the authors have reported suitable prescriptions. The study aims to raise awareness of them in order to gain the support of modern practitioners because of their easy accessibility, safety and low cost.

Conflicts interests

The authors declare no competing interests

Authors' contributions

Swedi M E collected the plants and did their preparation.

Tshilombo K F, Banza C L, Odimba B E made a substantial contribution to data analysis and interpretation, and to the correction of this article.

Arung K W is the promoter of the overall work and the main supervisor. Kasali M F and Bakary A S are professors of pharmacy at the Official University of Bukavu and the University of Lubumbashi, respectively, and have helped set the dosage of the phyto-drug.

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References

1. Institut Européen des substances médicinales. Les plantes médicinales, 2015, 52.
2. Van Asseldonk B, Barkin J, Elterman D. Medical treatment of Benign Prostatic Hyperplasia. Can J Urol. 2015 Oct;22(suppl 1):7-17.
3. Poirier J. Hypertrophie bénigne de la prostate et son traitement médicamenteux. Thèse pour Doctorat d'État en Pharmacie ; avril, 2010, 100.
4. Laarman V, Cassamayon A, Bernard C, Souccar Th, Luu Cl, Curtay JP, Dupuis JM. Prostate: le protocole naturel. Santé Nature Innovation.SNI Éditions SA, Suisse ; octobre, 2013, 1-26.
5. Association canadienne des urologues. La voix de l'urologie au Canada. Hypertrophie bénigne de la prostate, 2014, 3.
6. Unnikrishnan R, Almassi N, Fareed K. Benign prostatic hyperplasia: Evaluation and medical management in primary care. Cleveland Clinic 2017. Cleve ClinJMed. 2017 Jan ; 84(1):523.
7. Wilt TJ, MacDonald R, Ishani A. β Sitosterol for treatment of benign prostatic hyperplasia: A systematic review. BJU International. 1999;83:976-983.
8. Alternative Medicine Review. Pygeum Africanum (Prunus Africana, African Plum Tree). 2002 ;7(1):71-74.
9. Haddad P. Palmier nain. Société canadienne de recherche sur les PSN, Université de Montréal ; Juillet 2006-septembre, 2009, 69.
10. Linet TL, Anjili CO, Mutiso J, Ingonga J, Kliige SG, Mngedzo M, *et al*. Solanum aculeastrum in Leishmania major infection in BALB/c mice. Experimental study. Iran J Basic Med Sci. Jan. 2015;18(1):64-7.1.
11. Pagano E, Laudato M, Griffo M, Capasso R. Phytotherapy of Benign Prostatic Hyperplasia. A Minireview. Phytotherapy Research 2013. Published Online Library (Wiley online library.com) DOI: 10.1002/ptr.5084:7.
12. Consommer Report Health, Best buy drugs. Evaluating Drugs Used to treat Enlargement Prostate. May 2012, 1-17.
13. Manderbacher S, Ponholzer A, Berger I, Marszalek M. Medical Management of Benign Prostatic Hyperplasia: Role of Plants Extracts. EAU (European Association of Urology), 2007, 197-205.
14. Manorajan Sahu, Ramesh Bhat, Kala Suhas Kulkarni. Clinical evaluation of Himplasia in Benign Prostatic Hyperplasia: an open Clinical Trial. Med Update 2003:(11):1S75-78.
15. Johnson TV, Schoenberg ED, Abbasi A, Ehrlich SS, Kleris R, Owen-Smith A, *et al*. Assessment of American Urological Association symptom score in two distinct populations.J Urol. 2009;181:230-7.
16. Tranduc Tho. Assesment of therapeutic effect of soft gel Crinum Latifolium for Benign Prostatic Hyperplasia. Hanoi, 2005, 1-41.
17. Chung Homa, Wai Linge Lin, Singh Leung Lui, Xun-Yuan Cal, Vivian Taam Wong, Eric Zia, *et al*. Efficacy and Safety of Chinese Herbal Medicine for Benign Prostatic Hyperplasia: a systematic review of randomized controlled trials. Asian Androl 2013 Jul ;15(4):471-482.
18. Olapade EO, Olapade CO, Olapade OC. Phytomedicines for treatment of Benign Prostatic Hyperplasia. Acta Hort. 597, ISHS, 2003.
19. Usunabun U, Okolie NP, Anyanwu OG, Adebgedi AJ. Phytomedical screening and proximate composition of Annona muricata Leaves. European Journal of Botany Plant Science and Pathology. 2014;2(1):18-28.

20. Abdulani M, Aji SA. Phytotherapy for benign prostatic hyperplasia. The Clinical Efficacy and Safety of the use of Prostacare in patiemnts with Mild to Moderate Lower Urinary Trct Symptoms. J Surgery. 2016;4(2):4.
21. Munyantwari AE, Kasali MF, Swedi ME, Arung KW. Phytothérapie tradipraticienne des troubles mictionnels chez le sujet masculin âgé de 50ans ou plus à Goma. Rev Afr Med&S no1 Vol 3 Juillet 2019, 92-98.
22. Musée de recherche botanique de Lwiro; Institut de Recherche Scientifique (IRS-RDC) Source: iNaturalist Research-grade Observations, 2018. Available on https://www.inaturalist.org/observations/11075522 [27].
23. Zubair M. Genetic and environnemental on polyphenols in Plantago major. Introductory Paper at the Faculty of Landscape. Planning, Horticulture and Agricultural Science, 2010, 1-30.
24. Hussan F, Mansour AS, Nazihahasma Hassan S, Nurul Tasmin Tengku Not Effendi Kamarudin Tg, Sili Balkis Budin, Faizah Othman(Malaysia). Antiinflammatory Propertyof Plantago major, Laef Extract Reduces the inflammatory reaction in Experimental Acetaminophen-Induced Liver Injury. Hindavi Publishing Corporation Evidence Based and Alternative Medecine, 2015, 7. Article ID 347861.
25. Telabotanica eFlore, la fibre électronique de Tela Botanica. Projet de numérisation de la flore de l'abbé Coste par le réseau TelaBot 2011. Juive, Ph 2017: 9.
26. Durand C. Échantillonnage. Département de sociologie Université de Montréal, 2002.
27. Rasolofonantenaina RR. Etude phytochimique et biologique des extraits des feuilles d'Astrotrichilia parvifolia (Médiaceae), une plante médicinale malgache. Thèse Madagascar, 2018, 1-140.
28. Hajjij Gh. Sceening phytochimique, étude toxicologique et valorisation pharmacologique de Matricaria chamomilla et de l'Ormenis mixta L(Asteraceae). Thèse pharmacie. Université Mohamed V Rabat, 2018, 1-230.
29. Aboyade O, Yakubu M, Grierson D, Afolayan A. Studies on the toxicological effect of the aqueous extract of fresh, dried and boiled berries of Solanum aculeastrum Dunal in male Wistar rats. Hum Exp Toxicol 2009 Dec;28(12):765-75.
30. Babey TR, *et al*. Traitement de l'hypertrophie bénigne de la prostate. Clinical Research Scientist, 2016.
31. Koné A. Détermination des valeurs usuelles des paramètres biochimiques: la glycémie, la créatinémie, l'urémie et les transaminases parmi une population dans le district de Bamako. Thèse de Pharmacie ; Bamako, 2018, 1-99.
32. De Kien F. Réactifs de diagnostic *in vivo* pour la détermination quantitative de ALAT(GPT) dans le sérum ou plasma sur les systèmes photométriques. 2019 https.://www.biolabo.fr>pdf.
33. Costa J. ALAT/GPT opt. Linear chemicals, S.L.U. Barcelone 2018; www.linear.es.
34. Conseil scientifique. Domaine de la santé. Le bilan biologique hépato-biliaire en médecine générale. GT Laboratoire, mise à jour, 2019, 1-6.
35. Decock C. La phytothérapie et le foie. Thèse-Lille 2018, 1-130.
36. Régnier C. Faibles perturbations des transaminases en médecine générale. Étude prospective des principales étiologies dans les régions annéciennes de mars à octobre 2010. Thèse Grenoble, 2011, 1-176.
37. Service de médecine de premiers secours. Élévation des tests hépatiques. Hôpitaux Universitaires Genève-DMCPRU-HUG, 2017, 13.
38. Pillon J. Acide urique sanguin bas ou élevé: symptômes et alimentation. https.://www.passeportsante.net>fiche. 2019.
39. Saverne S. L'acide urique une molécule pouvant être pathologique. Thèse de Pharmacie-Limoges, 2013, 1-235.
40. Tanwi Priya, Shashank Maurya, Kishwar Hayat Khan. Cholestérol: genetic, clinical and naturel implications. Research Journal of Pharmaceutical, Biological and Chemical Sciences ; July september 2013;4(3):1-224.
41. Voisin M. Étude du métabolisme du cholestérol dans la progression et la résistance des cancers mammaires et identification des nouvelles cibles thérapeutiques. Thèse Toulouse, 2019, 1-271.
42. Akram Akhtar S. Prise en charge de l'hypercholestérolémie dans la prévention cardiovasculaire par les produits naturels. Thèse Lille, 2017, 1-85.
43. Masqood Zubair. Prescription des statines en soins primaires d'après les données scientifiques actuelles. Thèse Paris. 2014;(7):1-187.
44. Ninaemeka MU, Mgbekem MA, Eteng MU. Evaluation of Ocinum gratissimum Leaf Extrat on Lipid Profile of Experimental-Induced Prostatic Hyperplasia Animal Model. Journal of Advances Medical and Pharmaceutical Sciences. 2018;17(3):1-8.
45. Asteer Abd-Elnecor V. Hypoglycemic and Hypolipidic Effects of Pumpkin Seads Powder and Oil on Alloxan-Induced Diabet Rats. Egyptian Journal of Food Sciences. 2019;47,N°2:255-269.
46. Camara A. Facteurs associés au mauvais contrôle de la glycémie dans une population des diabétiques type 2 de l'Afrique subsaharienne. Thèse Rennes, 2014, 1-149.
47. Hatich N. Diabète type 2 et glycémie: qu'elle répartition idéale des repas en termes d'apport énergétique ? Travail de Bachelor. Haute Ecole de Santé, Genève, juillet 2017: 1-83.
48. Kojiro G Th. La protection cellulaire, les radicaux libres, les pathologies radiculaires, l'influence des suppléments sur ces pathologies. Flammarion, 2017.
49. Direction de la lutte contre les maladies. Normes directives de la prise en charge du diabète sucré type 2(RDC), 2015, 72.
50. Mubenga MLE. Association Hypertrophie bénigne de la prostate et diabète type 2 au Sud-Kivu(RDC), Thèse. Belgique, 2019, 178.
51. Monteil L3, Reynaud Th RVU-AGM: L'adénome de la prostate. Stratégie thérapeutique. Rein et voies urinaires-Appareil génital masculin (Pr Bastide) ; Marseille 2015: 10.
52. Haute Autorité de Santé (HAS). Rapport d'évaluation technique-Traitement des symptômes du bas appareil urinaire liés à l'hypertrophie bénigne de la prostate par laser ; novembre, 2013, 1-202.
53. Collège Français des Urologues. Item 123(Item247) - Hypertrophie bénigne de la prostate, 2014, 1-4.
54. ANAES/Service des recommandations professionnelles. Prise en charge de l'hypertrophie bénigne de la prostate. Mars, 2003, 1-94.
55. Seydou BM. Hypertrophie bénigne de la prostate au service d'urologie du CHU Gabriel Touré. Thèse doctorat d'Etat, Bamako, 2017-2018, 1-133.
56. Seisen Th, Evanguelos X, Roupet M, Robert G. Item 123-UE 5. Hypertrophie bénigne de la prostate. AFU, 2015, 18.
57. Duperron C. Hypertrophie bénigne de la prostate. CHU Dijon, 2007. https://fr.m.wikipedia.org>wikis.