



Prunus africana as Chemopreventive and Chemotherapeutic Agent for Prostrate Cancer: A Computational Approach

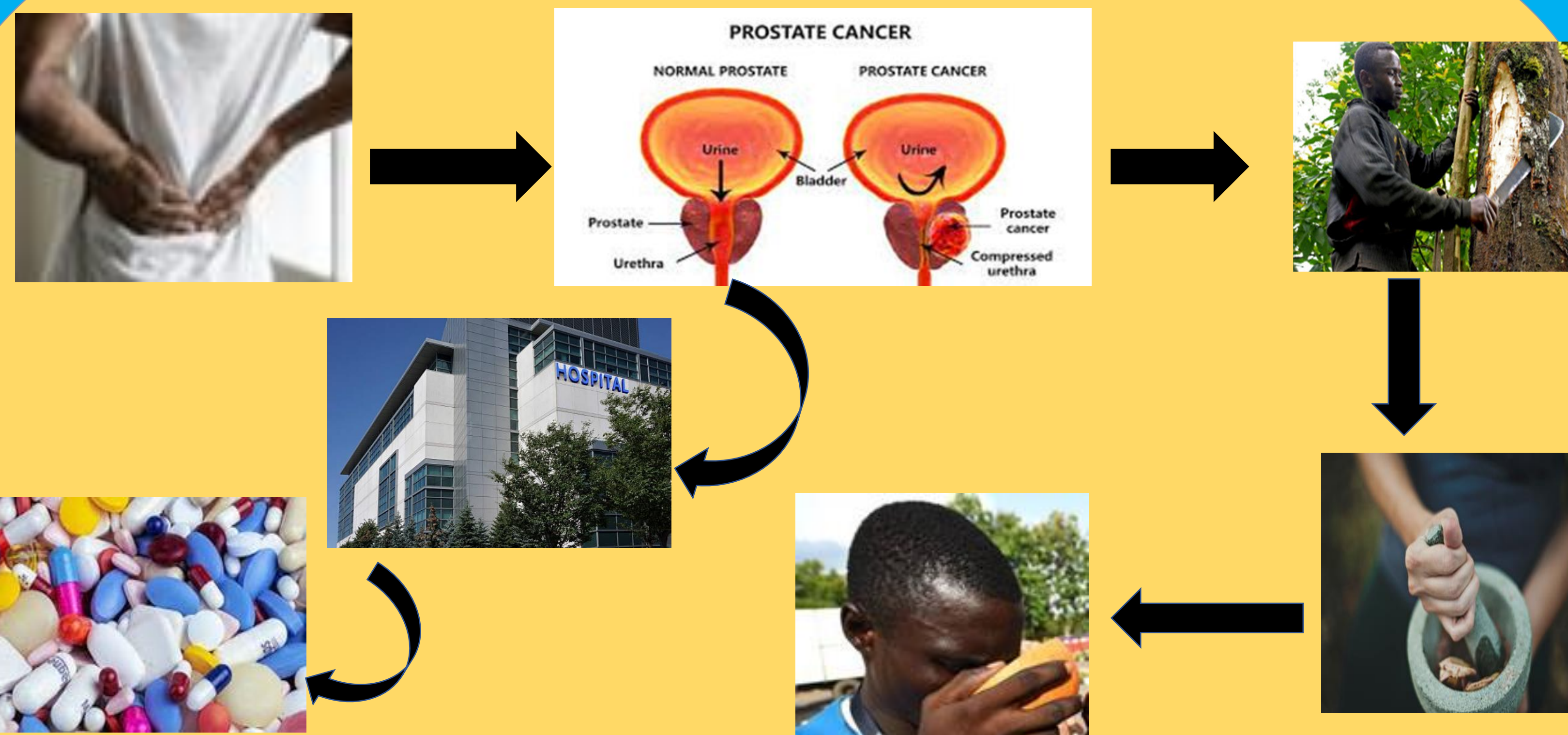
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Introduction



- Prostrate cancer is one of the most common tumours in the world. It is the leading cause of male death in Africa in general and Nigeria in particular.
- Prunus africana* has been used for generations in African traditional medicine to treat prostate cancer. [2]
- Insilico study of the phytochemicals of this plant is essential to verify claims by the traditional medicine practitioners that it prevents as well as cures prostrate cancer without side effects as against the standard drugs.

Problem Statement

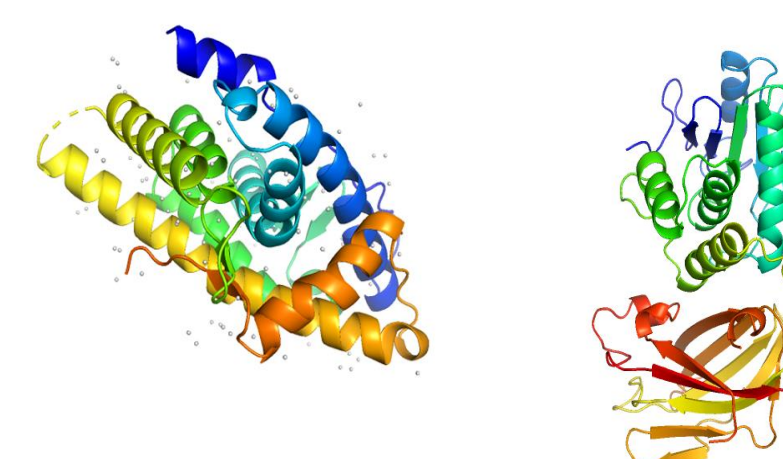


- Number of men with prostrate enlargement which could be benign or malignant are common
- Visit to hospitals at early stage of the ailment to ascertain nature of growth is poor
- They prefer treatment using herbs but come running to the hospital when critical
- Thus the need to verify the effectiveness of these herbs as claimed by the traditional medicine practitioners

Computational Details

12
Phytochemical
s of *P. Africana*
from Literature

- Pharmacokinetic study
- Molecular docking



AR and PTEN

5 Commercial
Drugs eg.
Flutamide
Bicalutamide etc.

- Phytochemicals with best binding energies where then analyzed for
- Bioactivity score,
 - Residue interaction
 - ADMET properties
 - Molecular properties

Results

Table 1: Activity Prediction

	PCAT		ANAT		PI		AEI		AA		PDT	
	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi
URA	0.329	0.034	0.145	0.015	0.764	0.005	0.557	0.018	0.890	0.004	0.266	0.062
OLA	0.417	0.019	0.104	0.022	0.752	0.005	0.645	0.008	0.901	0.004	0.294	0.053
BEA	0.510	0.009	0.156	0.014	0.761	0.005	0.723	0.004	0.923	0.004	0.315	0.044
BST	0.257	0.053	0.480	0.005	0.430	0.165	0.374	0.048	0.660	0.019	0.632	0.009
FLU	0.322	0.036	0.291	0.009	-	--	0.252	0.097	-	-	-	-
BCA	0.508	0.009	0.731	0.003	-	---	--	--	-	-	-	-
RFL	0.252	0.055	-	-	0.668	0.020	-	-	0.212	0.203	0.810	0.003
MK2	-	-	-	-	-	-	-	-	-	-	-	-
BPL	0.342	0.032	-	-	-	-	-	-	-	-	-	-

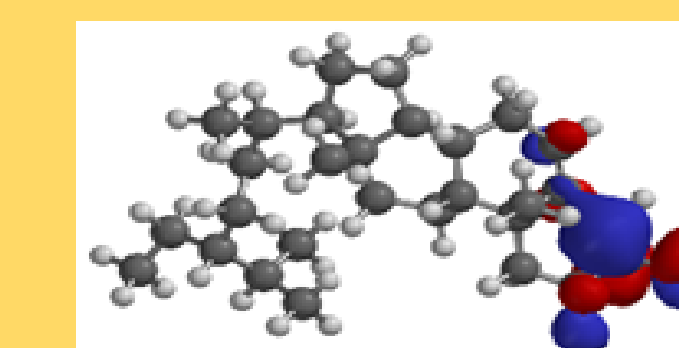
Pa: Probability activity, Pi: Probability inactivity PCAT: Prostrate cancer treatment, ANAT : Androgen antagonist, PI: Phosphatase inhibitor AEI: AR expression inhibitor, AA: Apoptosis agonist, PDT: Proliferative disease treatment.

Discussion

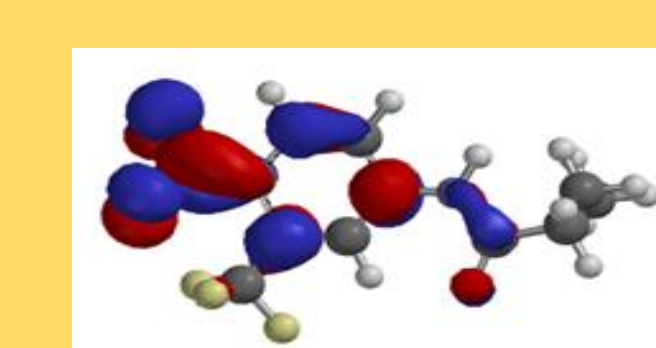
1. Pharmacokinetics and Toxicity Studies

- Based on the high probability of activity score (Table 1) for each of the process, only 4 constituents from *P. africana* exhibited chemotherapeutic and chemopreventive potential against prostate cancer.
- Some of its constituents showed good druglikeness and bioactivity
- Toxicity and pharmacokinetic studies revealed that some of the constituents of the plant extract had high risk of mutation, tumor generation, and irritation.

2. Quantum Chemical Studies



(A)



(B)

From the frontier molecular orbital calculations, the energy gap of the standard drugs were lower than that obtained for the *P. africana* phytochemicals, an indication that the former could be more reactive than the latter.

Fig 1: LUMO and HOMO of A) Beta sitosterone, B) Flutamide

Conclusion

- The fact that *P. africana* constituents have good druglikeness and bioactivity, its use for the purposes of therapy and prevention is discouraged due to its lipophilic, low bioavailability, high LD₅₀, and positive BBB values, making its activity in the system unreliable and unpredictable.

References

- [1] <https://www.johnhopkinsmedicine.org>
[2] Komakech R., Kang, Y., Lee, J., and Omuja, F. 2017 *Evidence-Based Complementary and Alternative Medicine*, 2017: 1-10.