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The Development of Novel Bioprocess to Enhance the Synthesis, Characterization, and Activation of Withaferin-A from *Withania somnifera*

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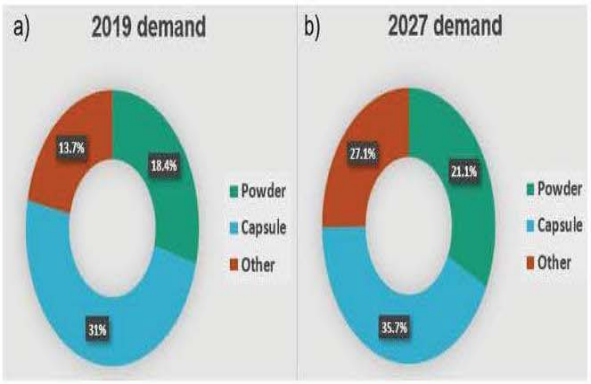
Abstract

Withania somnifera, commonly known as Ashwagandha, is a medicinal plant abundant in valuable triterpenoids, notably Withaferin A (WA), a potent bioactive compound found in the Northern Himalayas. Due to illegal wild harvesting and habitat disruptions, WA is now listed as a threatened species by the IUCN. With growing demand for Ashwagandha and its therapeutic compounds, biotechnological advancements are crucial for rapid yield enhancement. Recognized for its efficacy in treating conditions like breast cancer and COVID-19 (1), WA's purification and isolation from high-yielding endophytes are pivotal. Our objective is to identify hyperproducing endophytes and their enzymatic intermediates involved in withanolide synthesis, focusing on the MVA or MEP pathway related to sterols and terpenoids, facilitating Withaferin-A production. Cancer, originating from various organs and tissues, can metastasize and spread uncontrollably, often due to cancer stem cells within tumors. Chemotherapy failures and recurrences are linked to these cells. Our study screens Northern Himalayan endophytes for WA production, optimizing physical parameters and refining bioprocesses. Quality protocols ensure pure WA, while genetic analysis identifies synthesis markers. We evaluate WA's cytotoxic potential against cancer cells, bridging fundamental research with its therapeutic application in cancer treatment.

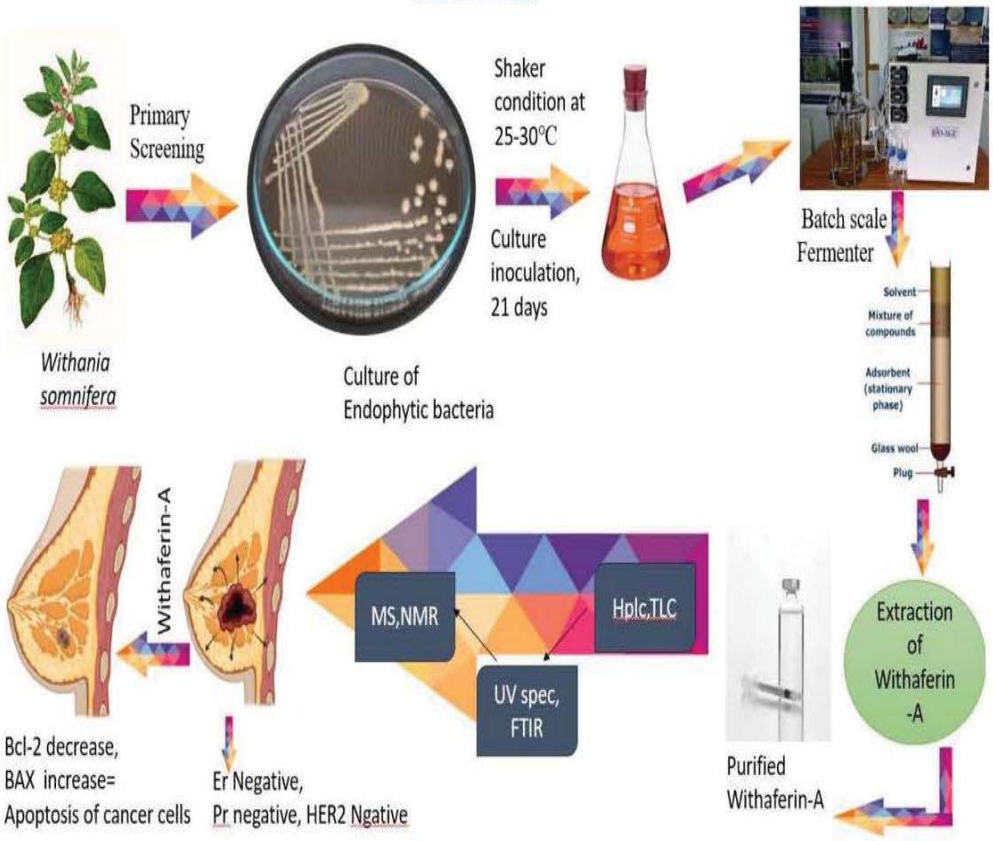
Keywords: Withaferin-A, Anti-cancer, Endophytes, Bio-active compounds

Introduction

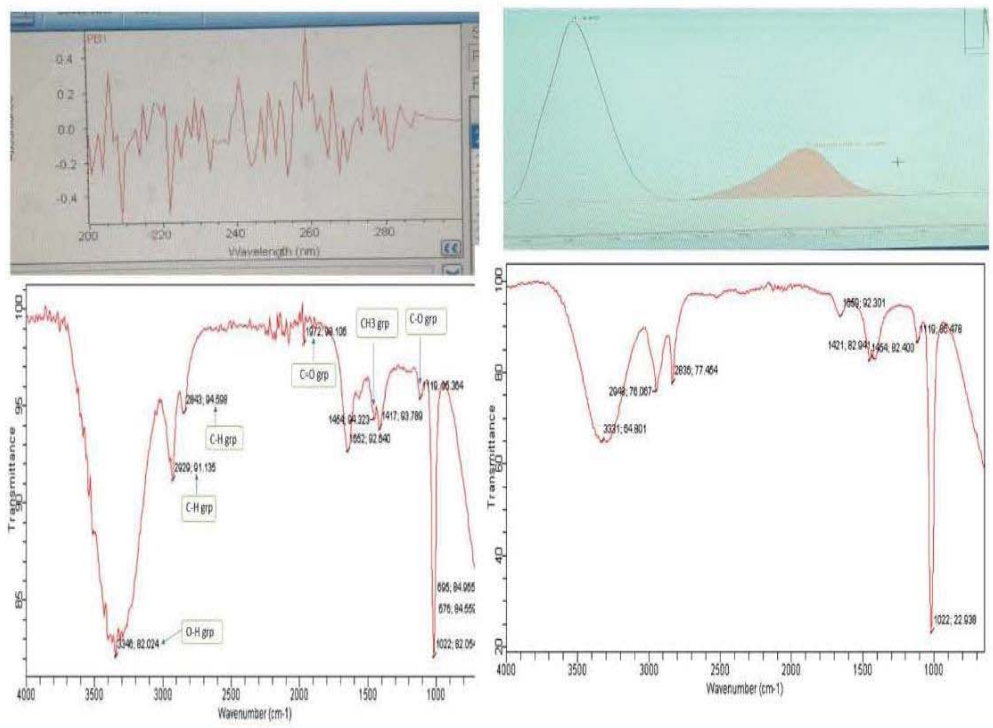
- Analysis by Data Bridge Market Research forecasts that the Ashwagandha market will reach USD 114.93 million by 2027, with an anticipated value of USD 46.75 million in 2022.
- Cancer involves uncontrolled cell growth due to genetic mutations, while normal breast cells respond to hormone levels via Estrogen and Progesterone receptors, regulating their growth.
- Triple Negative Breast Cancer (TNBC), a collection of breast tumors, is characterized by the absence of Estrogen and Progesterone receptor, and the overexpression of the (HER-2) gene, necessitating chemotherapy due to the absence of these targets.
- Due to its aggressive nature, TNBC often responds well to chemotherapy. Treatment is correspondingly aggressive to treat cancer and potentially save lives.
- Endophytes from plants are significant metabolite producers and can produce novel bioactive compounds.
- WA, sourced abundantly from the microbial-rich Himalayan Mountain range in the Indian Subcontinent, shows promise in treating aggressive cancers.
- Endophytes are rich sources of novel natural compounds and we are the pioneers for reporting bacterial endophytes which hyperproduce Withaferin-A.
- Short growth phase and ease of preservation can substantially improve productivity.
- Develop eco-friendly, cost-effective compounds through innovative optimization methods for bench-scale production, enhancing sustainability.
- Mutations and rDNA techniques could enhance production.



Methodology



Results



Conclusions

- Pioneer reporting bacterial endophytes producing Withaferin-A
- Focus on eco-friendly, cost-effective compounds
- Employ innovative optimization for bench-scale production

References

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Publications

- **Naimi Sirjohn**, Pradeep Kumar. *Withania somnifera* as a Prospective Therapeutics: Projecting the Present Situation and Upcoming Prospects. Critical Reviews in Biotechnology. I.F.9.062. Accepted.