Enhanced biosynthesis of bacoside from *Bacopa monnieri* by molecular biotechnology approach

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Medicinal plant-based drugs have been in huge demand and obtaining popularity in our routine life because they are convenient to access and possess minor side effects compared to synthetic drugs. *Bacopa monnieri* is an essential medicinal plant comprising of few pharmacological properties that incorporate memory enhancer, immunomodulator, adaptogen, anti-inflammatory, brain activator. Bacosides are triterpenoid saponins of the dammarane class that are considered as main constituent of this plant. This plant comparatively produces a very less quantity of bacoside and a huge amount of biomass is exploited to overcome the shortage in the pharmaceutical industry which hinders the optimal utilization of bacoside. Traditional bacoside extraction techniques are prolonged and impractical process, paving the path for the evolution of alternative biotechnological technologies that would enhance the production, scaling up and extraction process. Although various investigations have been performed in mass production using a biotechnological approach, limited research has been conducted on elucidating and determining the essential enzyme that governs biosynthesis of bacoside pathway. The current study focuses on the progress and prospects in numerous biotechnological and molecular aspects for meeting the worldwide demand for bacoside as well as highlighting these tools so that a platform for enhanced bacoside production may be constructed.

Keywords: Bacoside, *Bacopa monnieri*, Plant tissue culture, Transgenic plant, Bioreactor, Key genes

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Introduction

- ***Bacopa monnieri*** frequently identified as **"brahmi"** is an amphibious plant of tropics, commonly found growing on the banks of waterways and lakes the Indian subcontinent and graded second in the list of most vital Indian medicinal herbs.
- The plant is very popularly known as **"memory enhancing drug"** and has potential to treat neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease.
- The principal constituent of this plant is **triterpenoid saponins** of dammarane type known as **bacosides**.

Figure 1: field grown *Bacopa monnieri*

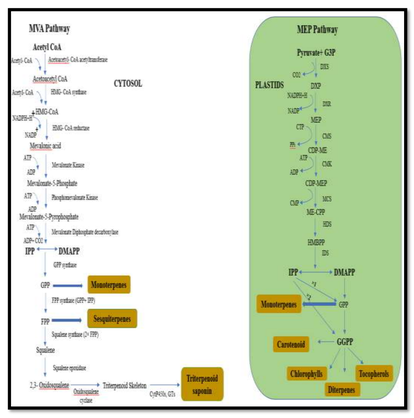


Figure 2: bacoside biosynthesis pathway

Background of study

- The enhanced commercial interest in bacosides has resulted in increased extraction of this herb which resulted in adding this herb to list of **endangered plant species**.
- These compounds are synthesized naturally in a very small quantity, thus purification from biological material gives rise to a very low yield, impurities and utilizes an exceptionally high measure of biomass.
- Thus, there is a need to develop alternative methods to enhance its production and conserve the plant. Plant tissue culture can increase the multiplication rate of cultures and thus reduces the cost, energy and labor requirements in commercial propagation of plant.
- It approvals the bulk propagation of plants in controlled environmental conditions without any seasonal constraints

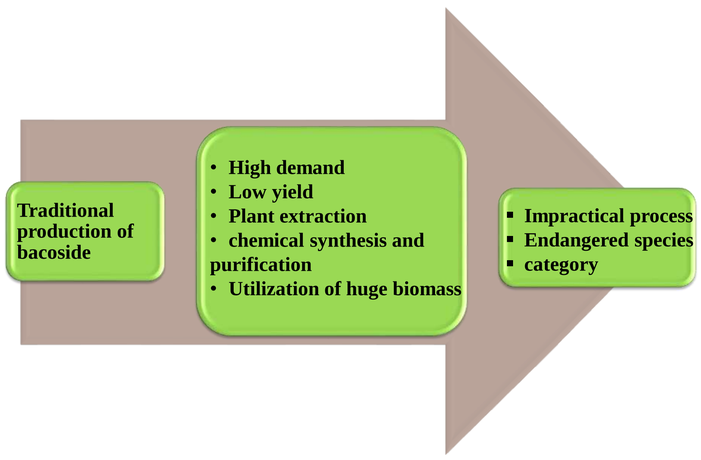
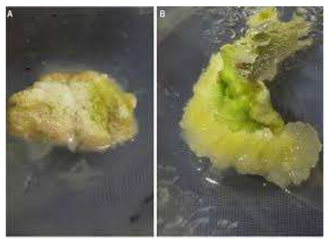


Fig 3: Drawback of traditional production of bacoside

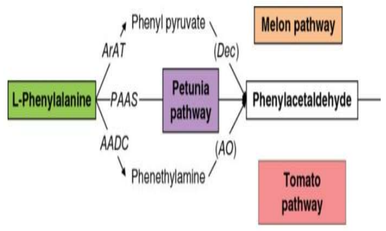
Objectives

- Production of bacoside using various tissue culture approaches
- Gene elucidation of bacoside biosynthesis pathway
- Establishment of large scale bioreactor to improve the yield of bacoside

Biotechnological and tissue culture approaches of bacoside synthesis



Elicitation



Precursor feeding

Field grown plant

Hairy root culture

Medium composition and culture condition

Bioreactor

Figure 4: Various approaches to improve production of bacoside in *Bacopa monnieri*

Process flow with enhancement strategies

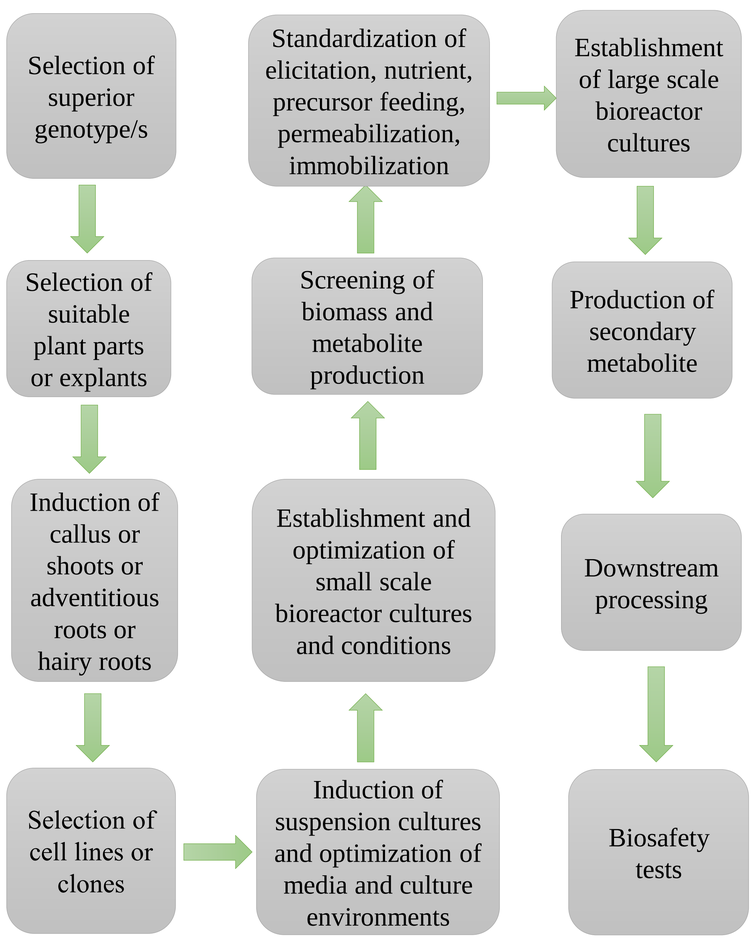


Table 1: Production of bacoside from *Bacopa monnieri* using different yield improvement method

Culture System	Yield improvement approach	Bacoside content	Reference
Cell suspension	Elicitation (salicylic acid)	6.58 mg g−1 DW	Koul and Mallubhotla, 2020
Cell suspension	Precursor (mevalonic acid)	11.88 µg/g DW	Hegazi et al., 2017
Hairy root	Hairy root	10.02 mg g−1 DW	Bansal et al., 2015
Shoot culture	Bioreactor (balloon type bubble bioreactor)	9.34 mg/g DW	Sharma et al., 2019
Cell suspension	Medium optimization	9.84 mg g−1 dry weight	Bansal et al., 2017
Shoot culture	Bioreactor (airlift bioreactor)	10.15 mg/g DW	Sharma et al., 2015
Shoot culture	Elicitation (salicylic acid and methyl jasmonate)	7.71 mg/g DW	Largia et al., 2016

Table 2: Genes isolated and characterized from *Bacopa monnieri*

Name of genes	Accession no.	Annotations	References
Acetyl-CoA C-acetyltransferase	FJ947159	BmAACT	Vishwakarma et al. (2013a)
Mevalonate kinase (MK)	JQ670899	BmMK	Kumari et al. (2014)
Mevalonate-5-pyrophosphate decarboxylase (MVD)	FJ947159	BmMVD	Abbassi et al. (2015 , 2016)
Farnesyl diphosphate (FPP) synthase	GU385740	BmFPS	Vishwakarma et al. (2012)
Squalene synthase (SQS)	GU734711	BmSQS	Vishwakarma et al. (2015)
Oxidosqualene cyclase (OSC)	HM769762	BmOSC	Vishwakarma et al. (2013b)
Glycosyltransferases (GTs)	FJ586244	BmGT,UGT74W1	Sharma et al. (2011) and Ruby et al. (2014)

Conclusion

- The recent developments in plant tissue culture techniques and bio-processing have shown promising results to improve biomass growth and the productivity by several folds.
- A complete study on the factors which controls the production of bacoside will maximize the yield and pave way for its successful commercialization.

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