Biotransformation of artemisinin mediated through fungal strains for obtaining derivatives with novel activities

Suchita Srivastava[1], Suaib Luqman[1], Atiya Fatima[2], Mahendra P Darokar[1*], Arvind S Negi[2], J K Kumar[2], K Shanker[2], Chandan S Chanotiya[2], Sudeep Tandon[3], Suman PS Khanuja[1]

[1]Genetic Resources and Biotechnology Division,
[2]Analytical Chemistry Division, [3]Process and Product Development

Central Institute of Medicinal and Aromatic Plants, Lucknow-226015, India.

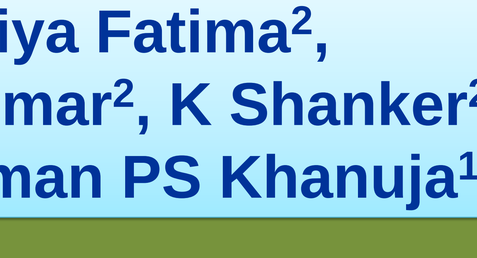
INTRODUCTION

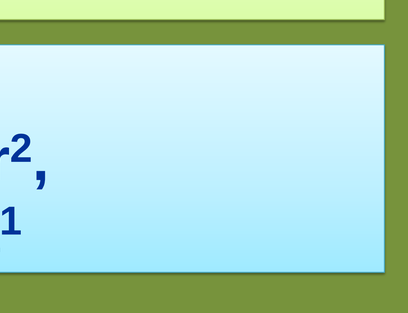
- Biotransformation: Process of modifying any organic compound into more water- soluble form using organisms
- It is an emerging field of biotechnology and encompasses both enzymatic and microbial biocatalysis
- Ecofriendly as they are less damaging to the environment than the chemical processes
- Microbial cells accepts a wide array of molecules as substrates yielding products with unparallel chiral, positional and chemical selectivity through various biochemical reactions.
- Microorganisms are exceptionally attractive models for studying fundamental life processes *in vitro*.

Artemisia annua

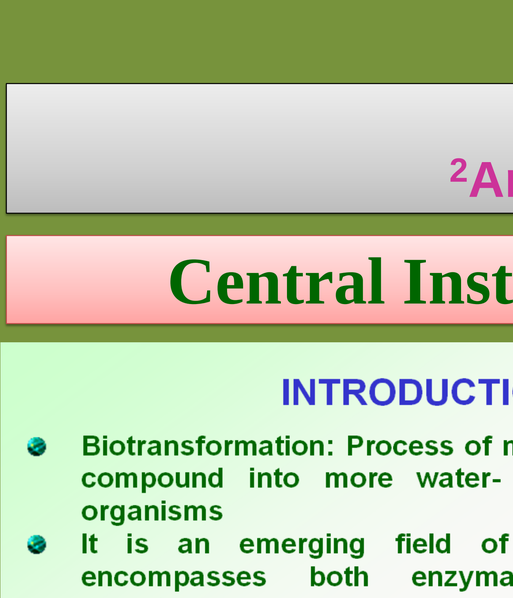
- *A. annua* L., is one of nearly 400 species of the Asteraceae family and commonly known as Sweet Wormwood, Sweet Annie, or Chinese wormwood.
- The herb is native to Asia but now grows in nature in many other countries in Europe and North America.
- *Artemisia annua* has chromosome number 2n=36 and having C value of 3.50 pg.
- Artemisinin is found in the glandular trichome of the leaves, stems, and inflorescences.
- The sesquiterpene lactone artemisinin accumulates to levels of 0.01–1% of dry weight.

Artemisia Biovillage





EXPERIMENT



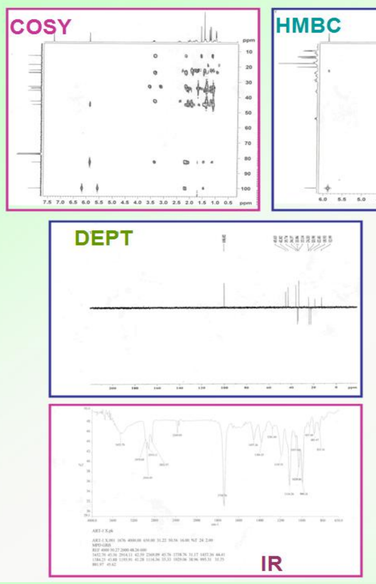
TLC
$_1H^1$ NMR
Preparative TLC
Scale Up
Column
C^{13} NMR
DEPT
COZY
HMBC
HSQC
HPLC

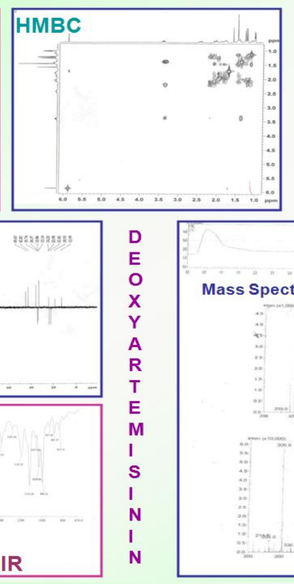
RESULTS

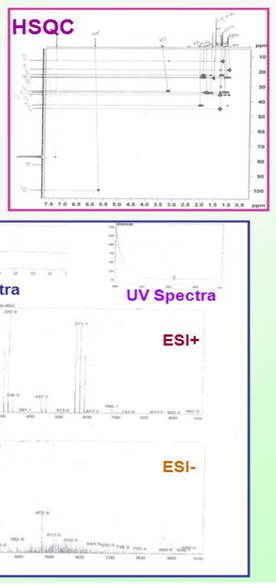
Table 1: ^1H and ^{13}C NMR data of 1 and 2 (both in $CDCl_3$, δ values) a,b

Assignment	Artemisinin (1)		Deoxyartemisinin (2)	
	^{13}C	^1H	^{13}C	^1H
1	50.17	1.40 (m)	45.10	1.27 (m)
2	24.87	1.47 (m), 2.03 (m)	22.43	1.23 (m), 1.88 (m)
3	35.96	2.43 (ddd), 2.07 (ddd)	34.41	1.59 (m), 1.77 (m)
4	105.32	--	109.51	--
5	93.68	5.87 (s)	100.01	5.88 (s)
6	79.48	--	82.80	
7	45.05	1.77 (m)	42.88	2.44 (dt)
8	23.39	1.88 (m), 1.12 (m)	23.90	1.07 (m), 1.88 (m)
9	33.66	1.81 (m), 1.09 (m)	33.91	1.11 (m), 1.77 (m)
10	37.63	1.43 (m)	35.75	1.24 (m)
11	32.89	3.38-3.42 (qd)	33.13	3.39 (distorted quartet)
12	171.82	--	171.97	--
13	12.49	1.23 (d, 7.2 Hz)	12.93	1.21 (d, 7.2 Hz)
14	19.74	0.99 (d, 6.0 Hz)	18.87	1.01 (d, J=6.0 Hz)
15	25.15	1.46 (s)	24.28	1.46 (s)

a Assignments are based on DEPT, 1H-1H COSY, HSQC and HMBC experiments.
b Signal multiplicity and coupling constants (Hz) are in parentheses.



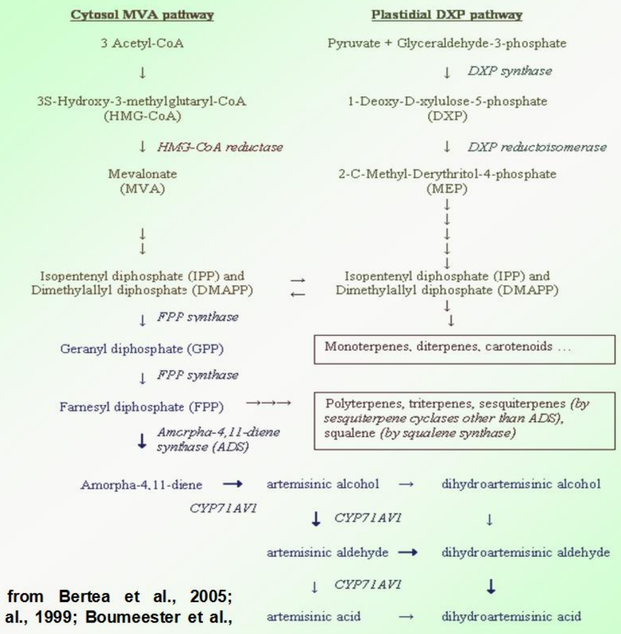




DEOXYARTEMISININ

Table 2: Minimum inhibitory concentration (MIC) of artemisinin and deoxyartemisinin against *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Streptococcus mutans*.

Pathogenic Bacteria	Minimum Inhibitory Concentration (mg/ml)	
	Artemisinin	Deoxyartemisinin
Staphylococcus aureus	>2	1
Staphylococcus epidermidis	>2	1
Streptococcus mutans	>2	1



(Adapted from Bertea et al., 2005; Wallart et al., 1999; Boumeester et al., 1992)

CONCLUSION

- The formation of the deoxyartemisinin suggests that *A. flavus* has the potential to serve as a microbial model for generating metabolites of artemisinin and its related analogues for the structural identification and for further use in investigating pharmacological and toxicological properties
- The biological activity obtained with deoxyartemisinin provides preliminary information for the design of novel antibacterial agents.

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