

**Bioprospecting of *Canscora diffusa* (Vahl) R.Br. Ex Roem.
& Schult. for the evaluation of phytochemical utilities with respect to
neurological ailments**

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ABSTRACT

Canscora diffusa (Vahl) R.Br. Ex Roem. & Schult. (Gentianaceae) is traditionally used in the treatment of nervous ailments such as memory loss, schizophrenia, and insanity. Due to limited availability and potential pharmacological significance, in vitro systems of *C. diffusa* were established. Shoot cultures of *C. diffusa* were successfully established in the solid Murashige and Skoog (MS) medium supplemented with 6-benzylaminopurine (0.2 mg/l) and 1-naphthaleneacetic acid (1 mg/l). In addition, adventitious root cultures were established in the liquid medium supplemented with indole-3-butyric acid (1 mg/l). Highest biomass (31.22 ± 0.16 g/l dry weight), total phenolic contents (61.03 ± 1.96 mg gallic acid equivalent/g dry weight), and total flavonoid contents (43.84 ± 0.54 mg quercetin equivalent/g dry weight) were observed in the adventitious root cultures after 42 days of incubation. These root cultures led to the isolation of 14 xanthone aglycones. Among these, five xanthenes namely 5-hydroxy-1,2,3-trimethoxyxanthone; 1,5-dihydroxy-2,3-dimethoxyxanthone; 1,6-dihydroxy-3,5-dimethoxyxanthone; 1-hydroxy-3,7,8-trimethoxyxanthone; and 1-hydroxy-3,5-dimethoxyxanthone exhibited acetylcholinesterase (AChE) inhibitory activity. Kinetic and molecular docking studies proposed their mixed-type of inhibition. These dual-binding inhibitors provide improved treatment of Alzheimer's disease, as they not only increase the acetylcholine levels (by blocking the active site) but also decrease the aggregation of β -amyloid (by inhibiting peripheral anionic site). In addition, 1-hydroxy-3,7,8-trimethoxyxanthone and 1-hydroxy-3,5-dimethoxyxanthone showed monoamine oxidase B inhibitory activity. As these two xanthenes also inhibited AChE, they have an added advantage in the treatment of dementia associated with Parkinson's disease. Xanthenes of *C. diffusa* also showed antioxidant activities, which is a positive indicator in alleviating the neurodegeneration caused by oxidative stress. These xanthenes comply with Lipinski's and Veber's rules conferring their drug-likeness. Further, these xanthenes possess required pharmacokinetic properties for blood-brain barrier permeation rendering their potential application in the treatment of central nervous system diseases.

Keywords: Acetylcholinesterase inhibitory activity, blood-brain barrier permeation, *Canscora diffusa*, monoamine oxidase B inhibitory activity, xanthone