

A cytotoxic agent from *Strychnos nux-vomica* and biological evaluation of its modified analogues

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Abstract Although a number of chemicals have been isolated from *Strychnos nux-vomica*, only a few have been evaluated for their biological significance. As a part of our drug discovery programme for cytotoxic agents from Indian medicinal plants, a novel cytotoxic agent, loganin **1** was isolated from the fruit pulp of *S. nux-vomica*. The loganin **1** showed significant anticancer activity against the human liver (WRL-68), colon (COLO-320 and CaCo2), ovarian (PA-1) and breast (MCF-7) cancer cell lines. Loganin **1** was further chemically transformed into eleven semi-synthetic derivatives **2–12** of which 2',3',4',7-tetra-O-acetyl-6'-O-(3'', 4'', 5'')-trimethoxybenzoyl loganin **11** and 2',3',4',7-tetra-O-acetyl-6'-O-lauroyl loganin **6** derivatives showed eight, 13 and three times while 2',3',4',7-tetra-O-acetyl-6'-O-lauroyl loganin **6** showed equal, 13 and two times more activity against human suspension colon (CaCo2), adherent colon (COLO-320) and liver (WRL-68) cancer cell lines, respectively, than the known anticancer

agent, vinblastine. The other analogues (except **4**, **8** and **9**) and loganin also showed marginal to moderate anticancer activity against the five tested human cancer cell lines.

Keywords *Strychnos nux-vomica* · Loganiaceae · Loganin · Anticancer · Cytotoxic assay

Introduction

Strychnos nux-vomica L. (Loganiaceae), commonly known as Snake-wood or *nux-vomica* tree is grown extensively in southern Asian countries and widely used in Chinese folk medicine (Anonymous, 1976; Bisset and Phillipson, 1976). The dried seeds of this plant have been claimed to improve blood circulation and relieve rheumatic pain (Guizhi, 1996). Historically, this plant has been widely used in treating diseases, such as tumour and rheumatic arthritis (Yong, 1975). Since long dried seeds of *S. nux-vomica* are being used as one of the major ingredient in some commonly prescribed Chinese herbal remedies such as “Ping-xiao” capsule, “Ci-dan” capsule or “Ma-qian-zi” tablet in the treatment of liver cancer (Xu *et al.*, 2003). Phytochemical investigations resulted in the identification of alkaloids as major constituents of this species (Bisset and Phillipson, 1976). Further, few related studies confirmed that, to a great extent, these alkaloids are responsible for the pharmacological properties of *S. nux-vomica*, such as cytoprotective and antitussive activities (Yanna *et al.*, 1992).

Loganin **1**, an iridoid glucoside is the major constituent of *S. nux-vomica* fruit pulp (Bisset and Choudhury, 1974). Since long it has been used as precursor in the biosynthesis of indole alkaloids and antimicrobial (Graiku *et al.*, 2002), hepatoprotective (Handa *et al.*, 1986; Raj *et al.*, 1996;

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