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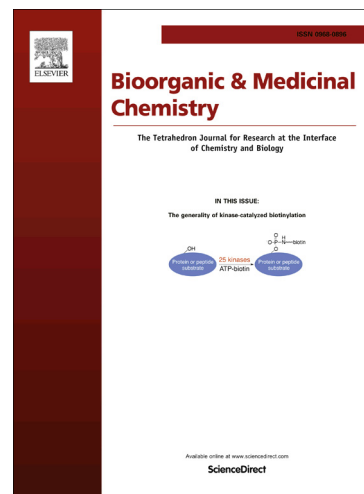
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## A one-pot laccase-catalysed synthesis of coumestan derivatives and their anticancer activity

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### Abstract

Suberase<sup>®</sup>, a commercial laccase from Novozymes, was used to catalyse the synthesis of coumestans. The yields, in some cases, were similar to or better than that obtained by other enzymatic, chemical or electrochemical syntheses. The compounds were screened against renal TK10, melanoma UACC62 and breast MCF7 cancer cell-lines and the GI<sub>50</sub>, TGI and LC<sub>50</sub> values determined. Anticancer screening showed that the cytostatic effects of the coumestans were most effective against the melanoma UACC62 and breast MCF7 cancer cell-lines exhibiting potent activities, GI<sub>50</sub> = 5.35 and 7.96 μM respectively. Moderate activity was obtained against the renal TK10 cancer cell-line. The total growth inhibition, based on the TGI values, of several of the compounds was better than that of etoposide against the melanoma UACC62 and the breast MCF7 cancer cell lines. Several compounds, based on the LC<sub>50</sub> values, were also more lethal than etoposide against the same cancer cell lines. The SAR for the coumestans is similar against the melanoma UACC62 and breast MCF7 cell lines. The compound having potent activity against both breast MCF7 and melanoma UACC62 cell lines has a methyl group on the benzene ring (ring A) as well as on the catechol ring (ring B). Anticancer activity decreases when methoxy and halogen substituents are inserted on rings A and B.

**Keywords:** Laccase, biocatalysis, coumestans, wedelolactone analogues, Michael addition, renal cancer, melanoma cancer, breast cancer, anticancer activity.

### Introduction

The coumestans, a class of naturally occurring compounds, have an interesting variety of biological activities such as antibacterial, antifungal, antimyotoxic, phytoestrogenic and phytoalexine effects.<sup>1</sup> Coumestans that have anticancer activity are wedelolactone (WDL) **1a**, demethylwedelolactone **1b**, psoralidin **2a**, coumestrol **2b** and their chemical structures are shown in Figure 1. The naturally occurring coumestan, wedelolactone (WDL **1a**, Figure 1), is a plant-derived natural product from the plant genus *Eclipta prostrata*, a Leguminosae.<sup>2</sup> *Eclipta* (or *Bhringaraj*) is a major source of WDL **1a**. This acrid and bitter herb has traditionally been used in medicine for hair and skin health and for preventing liver damage

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