Obtaining of (-)-hinokinin by catalytic oxidation of the lignan (-)-cubebin.

Karen C. S. Rezende[1] (PG), Alex L. Marcal[1] (PG), Guilherme V. Simaro[1] (PG), Thais E. Cintra[1] (IC), Mislaine A. Silva[1] (IC), Émerson H. Faria[1] (PQ), Kátia J. Ciuffi[1] (PQ), Jairo K. Bastos[2] (PQ), Wilson R. Cunha[1] (PQ), Márcio L. A. Silva[1] (PQ)*.

1 Universidade de Franca. Av. Dr. Armando Salles Oliveira, 201, Pq. Universitário, 14404-600, Franca-SP. 2 Faculdade de Ciências Farmacêuticas de Ribeirão Preto, FCFRP-USP. Av. do Café, s/n, 14040-903, Ribeirão Preto-SP.

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Introduction

Recent publications have highlighted numerous biological activities attributed to the lignans, specially (-)-cubebin (**1**), obtained of the seeds of *Piper cubeba*. Ongoing studies have focused on its structural optimization[1]. Green catalysts has been often employed to guide the performance of chemical processes in favorable conditions, without the formation of toxic sub-products[2]. The aim of this study is to obtain (-)-hinokinin (**2**) employing heterogeneous catalyst containing metalloporphyrin and iodosylbenzene as oxidant.

Results e Discussion

Oxidation of (**1**) were carried out using 100mg of (**1**), 100mg of KaAPTS + meso-tetrakis-(tetracarboxiphenyl)porphyrin) (KaAPTSFeTCPP), 100mg of iodosylbenzene, 2600µL of DCM:ACN 1:1 (v/v), magnetic stirring, room temperature, 48h, yielding 100%.

In order to determine the amount of (**1**) present or that which was consumed at different reaction times, a calibration curve was obtained through HPLC.

The obtainment of the product was analyzed in 2, 4, 8, 24 and 48 hours by HPLC. Reactions were also carried out in the absence of catalyst.

For reuse tests, after 48 hours, the reaction was centrifuged and to each solid decanted, 2600 uL of DCM:ACN 1:1 (v/v) were added, the suspension was kept under stirring for 30min and centrifuged again. The supernatant was discarded and the process was then carried out in the same manner. The catalyst was dried and the reaction was performed again.

The analyzes in HPLC were conducted on the binary system CBM-20A Shimadzu Prominence-LC-6AD equipped with a manual injector, a "degasser" DGU-20A5 coupled to a UV-Vis detector model SPD-20A, with data acquisition by a microcomputer, a Shimadzu analytical column, Shim-packODS, 250 x 4.20 mm, 5µm, equipped with pre-columns. The eluent system was formed from a mixture of methanol and water in a linear gradient 50% -100% in 20 minutes, λ 254 nm, 20µL, 1.0 mL/min.

It was possible to quantify the concentration of (**1**) by the peak area during the course of catalytic reactions.

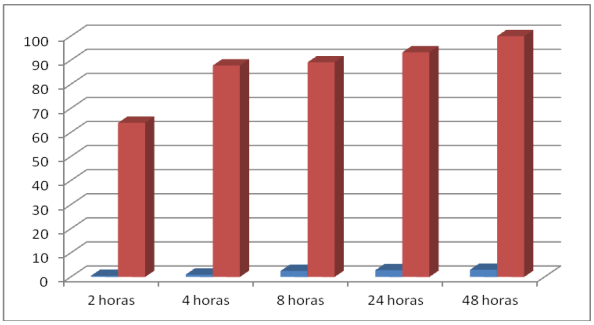

Figure 1. Obtainment of (**2**) during the time.

The oxidation mechanism catalyzed by porphyrin occurred by proton abstraction by the high-valence intermediate radical, iron(IV)oxo porphyrin-π-cation, Fe(IV)OP•+, formed by the interaction of porphyrin and iodosylbenzene.

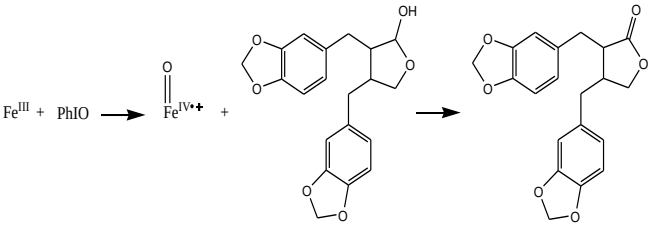

Figure 2. Mechanism of formation of (**2**).

Conclusions

It is concluded from the results, that the metalloporphyrin employed as the catalyst is a good biomimetic model of oxidation of (**1**) leading to formation of (**2**), a promising drug candidate, which can be employed to provide large amounts of samples for pharmacological and toxicological tests, aiming at large scale production in favorable environmental conditions.

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