Antioxidant and proapoptotic activities of *Sclerocarya birrea* [(A. Rich.) Hochst.] methanolic root extract on HepG2 and human dermal fibroblast cell lines

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It is well known that plant-derived antioxidant polyphenols can show both: prooxidative and antioxidative activities (Milella et al. 2014). Several studies indicated that among polyphenols, generally recognized as antioxidants, a wide range of them possess anticancer and apoptosis-inducing properties. These studies used both cancer cell lines and animal models of carcinogenesis (Gordaliza, 2007).

The aim of our study was to investigate the *in vitro* antioxidant activity and the apoptotic potential of methanolic root extract (MRE) of *Sclerocarya birrea* [(A. Rich.) Hochst.], better known as marula. It is a savannah tree belonging to the Anacardiaceae family and it has been identified as one of five fruit tree species that should be integrated in the domestication process because it is an important food and medicinal source for rural areas (Hamza et al. 2006; Jama et al. 2008). Different parts of the plant are traditionally used: the fruits are eaten or processed to make beer or jam; the kernels are eaten or used for oil extraction; the stem-bark, root, and leaf extracts of *S. birrea* are traditionally used against human ailments (Gouwakinnou et al. 2011). The content of polyphenolic compounds, mainly flavonoids and tannins, was determined. In order to evaluate the antioxidant activity, several *in vitro* assays were performed with particular regard to free radical scavenging activity. The cytotoxic effect of MRE was evaluated on the hepatocarcinoma cell line HepG2.

Our findings indicated that *S. birrea* MRE exhibits high amounts of phenolics, and it reported an important *in vitro* radical-scavenging activity. The MRE treatment induced apoptosis in HepG2 cells and generated reactive oxygen species (ROS) in dose-dependent manner. The cytotoxic effect promoted by MRE was prevented by pretreatment of HepG2 cells with N-acetyl-L-cysteine (NAC), suggesting that oxidative stress was pivotal in MRE mediated cell death. Both the loss of membrane potential and the release of cytochrome *c*, which ultimately contribute to typical morphological manifestations of apoptosis, (e.g., chromatin condensation and nuclear fragmentation) suggest that cytotoxic effect has triggered ROS-induced apoptosis in HepG2 cells. Result suggests that the apoptosis occurred in a mitochondrial-dependent pathway. Interestingly, MRE showed a sensibly lower cytotoxicity, associated with a low increase of ROS, in normal human dermal fibroblasts compared to HepG2 cells. This study demonstrated that compounds present in MRE, promoting ROS production, are able to interfere with cellular mechanisms specific of malignant cells. The presence of different classes of secondary metabolites detected in the extract provides a preliminary explanation of the experimental evidences, suggesting the needs for further investigation of MRE individual constituent effects (Armentano et al. 2015).

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