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### **PRELIMINARY ANTITUMOR AND HYPOXIA-SELECTIVE ANTIANGIOGENIC SCREENING OF SOME AFRICAN MEDICINAL PLANTS**

Emilie Bony<sup>1</sup>, Gabrielle Chataigné<sup>1</sup>, Julia Bensemoun<sup>1</sup>, Romain Boidot<sup>3</sup>, Thomas Genonceaux<sup>1</sup>, Robert Kiss<sup>2</sup>, Olivier Feron<sup>3</sup>, Joëlle Quetin-Leclercq<sup>1</sup>. <sup>1</sup>Pharmacognosy Research Group, LDRI, UCL, Brussels, Belgium; <sup>2</sup>Laboratory of Toxicology, ULB, Brussels, Belgium; <sup>3</sup>Institute of Clinical and Experimental Research, UCL, Brussels, Belgium.

The relationship between angiogenesis, cancer growth and metastasis has been well-established. Angiogenesis involves the proliferation and migration of endothelial cells which plays a crucial role in solid tumor development. Moreover, hypoxia is recognized as a hallmark of most tumor types, triggers angiogenesis and accounts for an increased resistance to anticancer treatments. Therefore, hypoxia is a highly selective parameter allowing the identification of new effective compounds in decreasing tumor proliferation without side effects on healthy tissues. Based on these considerations, we realized a screening of 25 African plants for antiangiogenic and antitumor activity by measuring the cytotoxic activity of 68 plant extracts on different cell types. The antiangiogenic activity was assessed on endothelial cells (HUVEC) both in hypoxic and normoxic conditions allowing the determination of a normoxia/hypoxia (N/H) ratio, and antitumor activity was evaluated on 3 different cancer cell lines (LoVo, PC-3, and U373). Among the 68 plant extracts screened, 9 exhibited a high hypoxia-selectivity with a N/H ratio  $\geq 2$ , the dichloromethane extract from *C. owariensis* being the most promising extract with a N/H ratio of 7.3 and high cytotoxicity on cancer cells. This study has demonstrated the successful use of hypoxia in the screening of plant extracts with antiangiogenic activity. Further fractionation of these crude extracts, which possess antitumor and hypoxia-selective antiangiogenic activity, is still required to identify new hypoxia-selective compounds.

### **PHYTOCHEMICAL INVESTIGATION OF WALNUT LEAVES ESSENTIAL OIL; ANTIOXIDANT EVALUATION USING VARIOUS METHODS**

Boukhari Fayçal, Tigrine-Kordjani Nacéra, Aliboudhar Hamza, and Geuzil Fatma Zohra. USTHB, Laboratoire d'Analyse Organique Fonctionnelle, Faculté de Chimie, Université des Sciences et de la Technologie Houari Boumediene, BP 32, El Alia, Bab Ezzouar, 16111 Alger, Algérie.

Leaves of *Juglans regia* L. have been widely used in folk medicine to cure many diseases including; venous insufficiency and haemorrhoidal symptomatology, and for their antidiarrheic, antihelmintic, depurative, and astringent properties. Most literature on the bioactivity of *J. regia* leaves has focused on their phenolics, but volatiles profiling was the subject of limited previous investigations, with little information on essential oil and its pharmacological effects. Thus in the present study, we contribute, for the first time, to elucidate the volatile constituents of fresh leaves of *J. regia* from Algiers region, using two different extraction methods: hydro-distillation assisted by microwave heating (MAHD) and classic hydro-distillation (HD), and the evaluation of their antioxidant Activity. Extraction time of 1 h with MAHD provided yields 0.05% (w/w) greater than HD yields 0.03% (w/w) obtained after 3 h. Analysis by GC-MS and GC-FID have shown similar qualitative composition, but a large difference in terms of contents of the constituents was observed<sup>1-2</sup>. Antioxidant capacity of the oil was evaluated by three different methods: the scavenging effect on DPPH radical (2, 2-diphenyl-1-picrylhydrazyl), reducing power (the ability of essential oil to reduce Fe<sup>+3</sup>) and  $\beta$ -Carotene/ linoleic acid bleaching assay (the ability of oil to inhibit the conjugated diene hydroperoxides arising from linoleic acid oxidation). The essential oil exhibited high antioxidant activity which was comparable to the reference standards at the same dose. These antioxidant properties are due to the chemical composition of essential oil that is rich in terpene and oxygenated terpene.<sup>3</sup>

<sup>1</sup>Boukhari *et al.* Helv. Chim. Acta (DOI: 10.1002/hlca.201200359), in press. <sup>2</sup>M. A. Farag JEOR (2008) 20: 323-327.

<sup>3</sup>Rather *et al.* Phytomedicine (2012) 19:1185– 1190.