

IN VITRO BIOLOGICAL ACTIVITIES OF ESSENTIAL OILS FROM THREE SUCCULENT PLANTS IN DRUG RESISTANT DISEASES

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Introduction: Succulent plants are adapted to dry environments where they may represent the only food resource and strong constitutive defenses are necessary to survive in their hostile habitat. Spines keep away large herbivores, but for microorganisms and arthropods chemical defenses are necessary. Essential oils (EOs) play a key role in plant defences and their biological properties are widely documented from a vast literature that demonstrates, among others, in vitro anticancer, anti-bioceptive, antiviral, antiphlogistic and antimicrobial activities. We tested the biological activities of the essential oils (EOs) of three succulent plants: *Cyphostemma juttae* (Vitaceae), *Alluaudia procera* (Didiereaceae) and *Kalanchoe beharensis* (Crassulaceae) in drug resistant diseases. This wide spectrum of biological activities is generally accompanied by biodegradability and reduced toxicity.

Material and methods: EOs were obtained by hydrodistillation, chemical composition determined by gas chromatography/mass spectrometry (GC/MS) analysis; cytotoxic activity by MTS assay, pro-apoptotic effect by staining with propidium iodide, ability to interfere with NF- κ B molecular pathways (TransAM NF- κ B assay, Real-Time PCR and Western blotting analysis) and antimicrobial activity by MIC evaluation. Results: We showed that *C. juttae* EO in two multidrug resistance cellular models, such as triple negative breast cancer cell lines (MDA-MB-231, SUM 149) caused a substantial decrease of NF- κ B activation and consequently a significant reduction of some NF- κ B target genes (antiapoptotic factors such as Survivin, XIAP, Bcl-2 and multidrug efflux transporter P-glycoprotein, encoding by ABCB1 gene). The same results were shown in HL60 leukemia cell line and in its multidrug resistance (MDR) variant HL60R, that in contrast to their parental cells lacked sensitivity to cell death induction from diverse stimuli including doxorubicin and cisplatin. These variant cells are characterized by overexpression of the ABC super family transporters act as ATP-dependent pumps, such as P-glycoprotein but also by constitutive expression of IAPs (inhibitor of apoptosis proteins) that play an important role in tumor cell resistance to drug induced apoptosis. Interestingly the EO of *K. beharensis* also induced a strong reduction of the NF- κ B molecular pathway in leukemia cell lines. Probably these pharmacological effects on multidrug resistance models are due to the high phytol content in EOs of *C. juttae* and *K. beharensis*. *A. procera* EO showed a similar pharmacological profile in leukemia cell lines but its antitumor activity is probably due to the high content in oxacycloheptadec-8-en-2-one. The presence of this macrolide compound induced us to test the potential antimicrobial property of *A. procera* EO. Indeed we observed an antimicrobial activity of the essential oil against multi-resistant bacteria such as *Staphylococcus aureus* and some resistant clinical isolates (2176 and 4668).

Conclusions: These results corroborate the idea that EOs can act as anticancer drugs. Further experiments will provide information on the possible chemosensitizing action of these EOs. The antimicrobial activity of *A. procera* EO deserves further investigations to confirm its possible use against drug resistant microorganisms.