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Brazilian natural products as a promising medicine for the treatment of inflammatory diseases and its nanoformulation

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During the development of new bioactive materials as tools for therapeutic use, one of the key questions is to understand how they interact with biological systems. In this way, it is essential to describe the mechanism of action aiming to understand how these materials induce their pharmacological effects and if these actions may cause health risks. New materials such as nanoparticles have attracted the attention of academy and industry. In particular, in Brazil we have researched several plant extracts and free or nanoencapsulated molecules for the treatment of inflammatory diseases using experimental models *in vitro* and *in vivo*. We have investigated the anti-inflammatory effect and toxicity of plant products, including imidazole alkaloids (Epiisopiloturine (EPI) and epiisopilosine (EPIIS) from Pilocarpus microphyllus Stapf), eugenol (a free or nanoencapsulated terpene) and dry extract of Amburana cearensis (microparticles). The EPI and EPIIS are side products in the Brazilian pharmaceutical industry which showed anti-inflammatory and antioxidant activities. Both alkaloids inhibited the degranulation of activated human neutrophils. This effect was accompanied by the reduction of ROS, the prevention of the increase of intracellular Ca2+ and decrease of the density of cytosolic NF-kB, and inhibition of TNF-α and IL-6 production. The EPI and EPIIS also inhibited carrageenan-induced inflammatory hypernociception in mice and reduced myeloperoxidase (MPO) levels. Eugenol (EUG) is a terpene present in essential oils of plants which has attracted attention due to its anti-inflammatory properties, as well as antioxidant effect. Despite of these pharmacological properties it presents irritant effect on skin which limit its use in topic, such as for treatment of dermatitis. To overcome it, we developed eugenol- loaded polymeric nanocapsules. The EUG, inhibited the ROS production in human neutrophil, but it was toxic in human keratinocyte and did not interfere with ear edema induced by TPA in mice. However, the nanocapsules of EUG (NCEUG) prevented its cytotoxicity in keratinocytes, and reduced ear thickness of mice (experimental model of dermatitis) reducing the MPO activity and the concentrations of IL-6 and KC (CXCL 1). Together, these results showed that NCEUG promoted a reduction in cytotoxicity of EUG and improved its anti-inflammatory effect. Parkinson's and Alzheimer's Disease are neurodegenerative diseases which neuroinflammation has an important role. Microglia is part of the innate immunity of central nervous system, being it activation one of the main mechanisms of inflammation responses. The standardized dry extract of A. cearensis (actives markers: coumarin and amburoside) reduced LPS-stimulated nitrite release on microglial and reduced the expression of iNOS (Western blot analysis). These findings suggest that molecules and/or plant extract from Brazilian medicinal plants, and its nanoencapsulation possess promising anti-inflammatory potential acting through the modulation of inflammatory response appear non-toxic.

Biography

Luzia Kalyne Almeida Moreira Leal is pharmacist and received her PhD in Pharmacology from the Federal University of Ceará, Brazil in 2006. She is Pharmacognosy professor at Federal University of Ceará since 1996. Her research interests are in Pharmacognosy and Pharmacology of Natural Products for the development of new medicines to treat inflammatory diseases. She is founder and coordinator of the Center of Pharmaceutical and Cosmetics Studies.

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