Nanoemulsão de licopeno da goiaba vermelha (*Psidium guajava* L) apresenta segurança in vivo, biodistribuição do licopeno e atividade citotóxica em células de câncer de próstata

Lycopene nanoemulsion from red guava (*Psidium guajava* L) display in vivo safety, lycopene biodistribution and cytotoxic activity on prostate cancer cells

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Lycopene is well-known antioxidant and it has been associated with protection against several disease. However, it can be degraded under exposition to light, oxygen and temperature variation, exhibits poor oral bioavailability and water solubility. As the nanobiotechnology has been an innovative alternative to improve the stability and biological activities of this compound, a nanoemulsion loading lycopene-purified from red guava, named nanoLPG, was produced. The nanoemulsion was characterized by dynamic light scattering (DLS), zeta potential and lycopene content over 12 months. The in vivo toxicity and tissue distribution were evaluated using male Swiss mice treated with nanoLPG at 10 mg/kg (test group) or water (control group) daily by oral route over 28 days. Clinical and behavioral, biochemical and hematological, and histopathological parameters were evaluated. The cytotoxicity on human prostate carcinoma cells (DU-145) was evaluated by MTT method. The statistical analyses were performed using the GraphPad Prism. NanoLPG exhibited polydisperse nanoparticles with an average diameter of around 200 nm; negative zeta-potential. The size, polydispersity index, and zeta potential parameters suffered insignificant alterations during the 12 months storage. Lycopene content in nanoemulsion analysis showed a statically significant (p<0.05) lycopene loss from the tenth month of storage at 5 - 8ºC. In contrast, the free LPG storage under the same conditions as nanoLPG presented total degradation in the first month. The animals exposed to nanoLPG at 10 mg/kg for 28 days did not exhibit abnormal clinical characteristics or change in general behavior, when compared with the water-treated animal. The evolution of body weight gain and the feed and water intake presented no significant changes. NanoLPG did not present hematological and biochemical change suggestive of in vivo toxic effect. The histopathological analysis of the brain, aorta, heart, lung, liver, spleen, kidney, stomach, esophagus, small intestine, large intestine, and pancreas revealed that nanoLPG did not induce pathological damage with clinical significance suggestive of toxicity at the experimental conditions. The lycopene from the oral administration of the nanoemulsion was detected in the prostate (0.03 ± 0.01 µg/g), kidney (0.11 ± 0.02 µg/g), and liver (0.18 ± 0.09 µg/g). The MTT assay demonstrated that the treatment with free LPG and nanoLPG significantly (p<0.05) affected cell viability after 6 hours of exposure even at the lowest concentration (3.125 µg/mL), with a reduction of 19.33 ± 2.36% and 44.65 ± 6.90%, respectively. The maximum effect for free LPG and nanoLPG was observed at 72 hours of exposure at 200 µg/mL (93.20 ± 0.31% and 100 ± 3.32% of viability reduction, respectively). In brief, nanoLPG present potential for application as nanotechnology-based product for lycopene delivery, emphasizing its in vivo safety and anti-cancer activity. We thank to Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, Brazil) for support and Laboratory of Food, Drug & Cosmetics (LTMAC) of the University of Brasília (UnB) for providing the equipment Zetasizer NanoZS90 (Malvern, UK).