Cytotoxic and genotoxic effects of essential oil from leaves of *Casearia sylvestris* Sw. (Salicaceae) on A549 tumor cell line.

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Casearia sylvestris Sw. belongs to the family Salicaceae, and can be found in all extension of Brazilian territory. This plant is included in the public health system (SUS) of Brazil. According to literature, *C. sylvestris* showed cytotoxic and genotoxic effects in different tumor cell lines and the anticancer potential of extracts could be due to casearins (clerodane diterpenes). On the other hand, there are few studies related to the antitumor activity of the essential oils from this species (1). This study aimed to evaluate the cytotoxicity and DNA strand break effects of the essential oil from leaves of *C. sylvestris* against A549 tumor cell line (human lung carcinoma). The botanical material was collected in Tijuca National Park and a voucher was deposited under the number RB 570651 at the Herbarium of the Research Institute of Botanical Garden of Rio de Janeiro. Fresh leaves (150g) were subjected to hydrodistillation in a Clevenger-type apparatus for 2 hours. The essential oil was diluted in dichloromethane and then analyzed by GC-MS and GC-FID (Agilent 6890N coupled to Agilent 5973N), equipped with HP-5MS fused silica capillary column (30 m x 0.25 mm i.d. x 0.25 µm); helium and hydrogen were used as carrier gas for GC-MS and GC-FID, respectively, with a flow rate of 1.0 $mL.min^{-1}$. Oven temperature was raised from 60 to 240°C at $3°C.min^{-1}$. Compounds were identified by comparison of both mass spectra and linear retention indices with spectral library and literature. For the cytotoxic and genotoxic assays, A549 cell line was used. Different concentrations of the essential oil (0.5, 1.0, 2.0 and 4.0 $\mu g.mL^{-1}$) were assayed to evaluate the cytotoxicity by wst-1 and clonogenic assay. DNA damage (genotoxicity) was evaluated by the comet assay (2). Results were expressed as the half-maximal response (EC_{50}). In total, 63 compounds were identified in the oil, comprising more than 90% of the mixture. Germacrene D (9.9%), viridiflorol (7.9%) and (*E*)-caryophyllene (5.4%) were identified as the main compounds. The essential oil showed cytotoxic activity against A549 tumor cells with EC_{50} at 4.0 $\mu g.mL^{-1}$ and showed dose dependent pattern ($r = -0.79$, $p = 0.03$) as determined by linear regression test. Genotoxicity assay showed DNA damages of types I – IV at 4.0 $\mu g.mL^{-1}$ according to the Damage Index (DI). Our results show that essential oil of *C. sylvestris* is rich in sesquiterpenes, displaying cytotoxic activity against tumor cell line A549, and promoting DNA damages.

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