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Why extracts of five Indian plants cure cancer: Enhanced protection of DNA but destruction of nucleotides through the endogenous fenton reaction, and inhibition of human topoisomerases

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The influence of substoichiometric amounts of seven plant extracts in the Fenton reaction-mediated damage to deoxynucleosides, dNMPs, dNTPs and supercoiled plasmid DNA were studied to rationalize anticancer properties reported in the extracts of *Acacia catechu, Emblica officinalis, Spondias dulcis, Terminalia belerica, Terminalia chebula.* Extracts from these five plants, as well as four pure compounds contained, enhance the extent of damage in Fenton reactions with all monomeric substrates but protect supercoiled plasmid DNA, compared to standard Fenton reactions. However, *Dolichos biflorus and Hemidesmus indicus* extracts generally do not show this enhancement for the monomeric substrates though they protect plasmid DNA. A catalytic mechanism involving the presence of a ternary complex of the nucleoside / nucleotide substrate, a plant compound and the hydroxyl radical was proposed [J. Biomol. Struct. Dyn. 2016; doi:10.1080/07391102.2016.1244493]. Such a mechanism cannot operate for plasmid DNA. These plant extracts will slow down DNA replication in rapidly dividing cancer cells. In another set of experiments, extracts of the same five plants completely inhibit human topoisomerase I at 40 µg/ml concentration while *Hemidesmus indicus* and *Dolichos biflorus* extracts inhibit partially. All seven plant extracts partially inhibit human topoisomerase II at 120 µg/ml concentration. Chebulagic and chebulinic acids purified from *Terminalia chebula* extract inhibited human topoisomerase I at around 2 µM and 3 µM respectively [Molecular Enzymology and Drug Targets 2017. Vol. 2. No. 2. http://www.imedpub.com]. The nuclear fragmentation leading to apoptosis observed earlier in cancerous cell lines with such plant extracts may thus be explained by the inhibition of topoisomerases.

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