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A REVIEW ON EFFECT OF CAFFEIC ACID ON HEPATOCARCINOMA

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ABSTRACT
Caffeic acid (CA) is a phenolic compound synthesized by all plant species and is present in foods such as coffee, wine, tea, and popular medicines such as propolis. This phenolic acid and its derivatives have antioxidant, anti-inflammatory and anticarcinogenic activity. In vitro and in vivo studies have demonstrated the anticarcinogenic activity of this compound against an important type of cancer, hepatocarcinoma (HCC), considered to be of high incidence, highly aggressive and causing considerable mortality across the world. The anticancer properties of CA are associated with its antioxidant and pro-oxidant capacity, attributed to its chemical structure that has free phenolic hydroxyls, the number and position of OH in the catechol group and the double bond in the carbonic chain. Pharmacokinetic studies indicate that this compound is hydrolyzed by the microflora of colonies and metabolized mainly in the intestinal mucosa through phase II enzymes, submitted to conjugation and methylation processes, forming sulphated, glucuronic and/or methylated conjugates by the action of sulfotransferases, UDP-glucotransferases, and o-methyltransferases, respectively. The transmembrane flux of CA in intestinal cells occurs through active transport mediated by monocarboxylic acid carriers. CA can act by preventing the production of ROS (reactive oxygen species), inducing DNA oxidation of cancer cells, as well as reducing tumor cell angiogenesis, blocking STATS (transcription factor and signal translation 3) and suppression of MMP2 and MMP-9 (collagen IV metalloproteases). Thus, this review provides an overview of the chemical and pharmacological parameters of CA and its derivatives, demonstrating its mechanism of action and pharmacokinetic aspects, as well as a critical analysis of its action in the fight against hepatocarcinoma.

Keywords:- *Caffeic acid, Hepatocarcinoma, Phenolic compound, carcinogenesis, UV- B*

INTRODUCTION

Caffeic acid (CA) is a polyphenol produced through the secondary metabolism of vegetables, including olives, coffee beans, fruits, potatoes, carrots and propolis, and constitutes the main hydroxycinnamic acid found in the diet of humans . This phenolic compound is found in the simple form (monomers) as organic acid esters, sugar esters, amides and glycosides, or in more complex forms such as dimers, trimers and flavonoid derivatives, or they may also be bound to proteins and other polymers in the cell wall of the vegetable. CA participates in the defense mechanism of plants against predators, pests and infections, as it has an inhibitory effect on the growth of insects, fungi and bacteria and also promote the protection of plant leaves against ultraviolet radiation B (UV-B).

In vitro and *in vivo* experiments have been performed, proving innumerable physiological effects of CA and its derivatives, such as antibacterial activity, antiviral activity, antioxidant activity , anti-inflammatory activity, anti-atherosclerotic activity, immunostimulatory activity, antidiabetic activity, cardioprotective activity, antiproliferative activity, hepatoprotective activity, anticancer activity, and anti-hepatocellular carcinoma activity. Among these properties, anti-hepatocarcinoma activity is highlighted, because hepatocarcinoma (HCC) is one of the main causes of cancer mortality in the world. Therefore, further studies on the chemical and pharmacological aspects of CA are necessary to contribute in the future to the development of a new drug and consequently the expansion of therapeutic possibilities. Thus, this review provides an overview of the chemical and pharmacological parameters of CA and its derivatives, reporting its main mechanisms of action and pharmacokinetic aspects, as well as to critically analyse its performance in the fight against HCC.

Chemical Aspects of Caffeic Acid

AC (3,4-dihydroxycinnamic acid) is a hydroxycinnamic acid, belonging to the phenolic acid family, which has a phenylpropanoid(C6-C3) structure with a 3,4-dihydroxylated aromatic ring attached to a carboxylic acid through a transethylene wire. The biosynthesis of this compound in plants occurs through the endogenous shikimate pathway that is responsible for the production of aromatic amino acids from glucose.