

## THERAPEUTIC ASPECTS OF CATECHIN AND ITS DERIVATIVES – AN UPDATE

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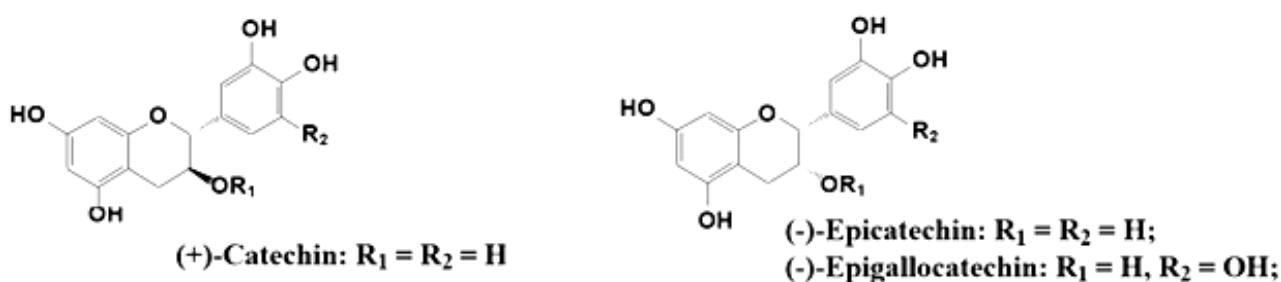
**Abstract:** Catechin and its derivatives are polyphenolic benzopyran compounds. The condensation of catechin units leads to the formation of condensed tannins. It is found in appreciable amount in green tea leaves, cocoa, red wines, beer, chocolate, etc. It possesses important antioxidant, antibacterial, antifungal, antidiabetic, anti-inflammatory, antiproliferative and antitumor properties. The present review outlines recent updates and perspectives of the effects of catechins and the pharmacodynamic mechanisms involved.

**Keywords:** catechin, antitumor, antioxidant, antibacterial, hypolipidemic.

### 1. Introduction

Catechins are flavanols which belong to polyphenolic compounds. Condensed or non-hydrolyzable tannins are formed by the condensation of catechin (epicatechin and a catechin epimer) (**Fig. 1**). Catechin, together with epicatechin and epigallocatechin gallate, are the main flavonoids which are found in the composition of green tea (Li et al., 2018). Many research results have highlighted that

catechins have an important role in protection against degenerative diseases (Ide et al., 2018). Other studies have demonstrated an inverse reaction between catechin intake and the risk of cardiovascular diseases (Ikeda et al., 2018). It has been reported that catechins appear to produce greater antibacterial activity against Gram-positive bacteria than Gram-negative ones (Ajiboye et al., 2016; Gomes et al., 2018).



**Fig. 1.** Chemical structure of catechin and its derivatives

The present paper is a critical review of the recent literature on therapeutic aspects and pharmacodynamic mechanisms of catechin and its derivatives.

## 2. Bioavailability and biological effects of catechin and its derivatives

The bioavailability of catechin and its derivatives differs significantly depending on the form under which it is found (**Table 1**). When administered in esterified form with gallic acid, the absorption is much slower. Methylated forms were identified as a result of metabolism in the case of epigallocatechin. In another study, the plasma concentration of 4'-O-methyl-epigallocatechin was determined, whose value was 5 times higher in plasma and 3 times higher in urine than the concentration of epigallocatechin (Rothwell et al., 2018). Epigallocatechin gallate is the only flavonol form which is present in plasma in a significant percentage (48-55%).

The other catechins are detected as the glucuronidated or sulphated form. The main epicatechin metabolites are: epicatechin-3'-O-glucuronide, 4'-O-methylepicatechin-3'-O-glucuronide, 4'-O-methyl-epicatechin-5- or 7-O-glucuronide, 4'-O-methylepicatechine and epicatechin aglycone (Liao et al., 2018; Casanova et al., 2019). Metabolization leads to metabolites that can extend the beneficial effect of catechins, having a longer half-life (5 hours for epigallocatechin-3-gallate). In this case, renal excretion of catechins is very rapid (Manach et al., 2005; Ikeda et al., 2018).

Catechin influences molecular mechanisms involved in angiogenesis, extracellular matrix degradation, regulation of cell motility, and multiple resistance to cancers and associated disorders.

Based on epidemiological and experimental studies, a correlation between green tea consumption rich in catechins and cardiovascular health has been highlighted by

several antioxidant, antihypertensive, anti-inflammatory, antithrombotic, hypolipidemic, etc. effects (Rothwell et al., 2018). It was also shown that catechin and its derivatives, namely epigallocatechin gallate, would inhibit platelet aggregation. These effects were explained by the inhibition of cytoplasmic calcium growth (Lill et al., 2003; Watson et al., 2014). Catechins also have an important role in maintaining homeostasis (Matsui, 2015), their cardioprotective and antidiabetic effects have been demonstrated by several studies (Thielecke et Boschmann, 2009; Hashemipour et al. 2017).

## 3. Antiallergic properties

New studies have been conducted on the anti-inflammatory and anti-allergic effects of catechin (Hussein et al., 2015). The pharmacological effects of catechin in mice with allergic rhinitis were determined by performing haematoxylin and eosin staining and Giemsa staining of the nasal tissues essential in observing the allergic symptoms. The results showed that catechin, at 75, 150 or 300 mg/kg bodyweight, reduced the allergic symptoms in mice with allergic rhinitis, such as sneezing and nasal rubbing. Catechin could reduce interleukin-5, interleukin-13 and ovalbumin E serum concentrations and restore T helper type 2 / T helper type 1 cell balance. Catechin has efficiently decreased the inflammation in allergic rhinitis. The mechanism of action would be that catechin inhibited the expression of TSLP (lymphatic stromal lymphopoietin) in epithelial cells by influencing the NF- $\kappa$ B / TSLP pathway (Pan et al., 2018).

## 4. Cardiovascular effects

Recent evidence demonstrates that catechins can be key mediators in cardiovascular health through mechanisms underlying blood pressure reduction,

vasodilation, and atherosclerosis (Mangels et al, 2017).

The prevalence of coronary heart disease in Asian people is demonstrated to be very low due to their increased tea consumption (Shahid et al., 2016; Li et al., 2018). Also, recent studies have demonstrated that, due to their antioxidant effect, they have the ability to reduce cytotoxicity produced by amiodarone (commonly used antiarrhythmic drug) in human lung fibroblast cells (Cooper et al., 2005; Santos et al., 2017).

### 5. Antioxidant and anti-tumor effect

Clinical trials conducted so far have shown the beneficial effects of catechin due to its antioxidant action. The ability of catechins to cross the blood-brain barrier has led to increased interest related to their antioxidant properties beneficial for the prevention and treatment of neurodegenerative diseases.

Catechin and other catechins in green tea block carcinogenesis and help modulate signal transduction pathways related to proliferation, transformation, inflammation and metastasis of cells. It also has a chemopreventive potential (Grzesik et al, 2018; Yang et al., 2018; Baranowska et al., 2018) and catechin nanohybrids significantly improve the anti-tumour effect by inducing apoptosis of WM266 human melanoma versus free catechin (Di Leo et al., 2017). Also, the loading of catechin with PLGA (poly (1-lactide-co-glycolide)) fibers had a high effect of reducing the reactive oxygen species, so processing of catechin in controlled release forms could allow future localized applications of great importance in the fields of tissue engineering and wound healing (Ghitescu et al., 2018).

Oxidative stress plays a central role in the degeneration of neurons by activating intracellular signaling cascades, which have a role in autoimmune apoptosis and extracellular modulation (Suryavanshi et al, 2017, Bhatt et

al., 2012) processes. Generation of ROS in neuronal cells activates inflammatory mediators like TNF- $\alpha$ , COX-2, NF- $\kappa$ B as well as proapoptotic mediators such as Bcl-2 and caspase-9 (Suryavanshi et al, 2017; Kimura-Ohba et al., 2016). Catechin directly or indirectly decreases neuronal damage by reducing oxidative stress, scavenging ROS and improving antioxidant enzymes (Shai et al 2015; Xiang et al., 2016).

### 6. Lipid-lowering effects

Studies in rats have shown that catechin in green tea can reduce the risk of cardiovascular disease (CD). The effect has been attributed to the antioxidant and anti-inflammatory properties of catechin. Also it is suggested that catechin reduces the risk of cardiovascular disease by lowering cholesterol and triglyceride levels (Cooper et al., 2005). In vitro and in vivo studies show that catechins in green tea inhibit intestinal absorption of dietary lipids, by interfering with lipid digestion and their solubilization (the critical steps involved in the intestinal absorption of dietary fats, cholesterol and other lipids). Based on the information available so far, it is clear that green tea and its catechins effectively reduce the intestinal absorption of lipids (Ikeda et al., 1992). The mechanism of action of catechin is based on the fact that it inhibits the absorption of lipids. This effect appears to be associated with its ability to form complexes with lipids and lipolytic enzymes, thereby interfering with emulsification, hydrolysis, micellar solubilization processes and subsequent absorption of lipids. These mechanisms are not fully clarified and further studies are needed to define mechanisms underlying lipid absorption inhibition (Shishikura et al.; 2006; Koo et al., 2007).

## 7. Antibacterial and antiviral effect

Polyphenols are among the most abundant compounds in the plant kingdom. They have been reported to be associated with a number of organoleptic properties of drinks and foods.

**Table 1.** The effect of catechin and its derivatives

Compound	Effect	Reference
epicatechin gallate	beneficial role in muscles	Kim AR et al., 2017
epigallocatechin-3-gallate	regeneration	
epigallocatechin, epicatechin, epigallocatechin-3-gallate, epicatechin-3-gallate	antioxidant cardioprotective	Ikeda et al., 2018
epigallocatechin gallate	antibacterial	Miyamoto et al., 2017
epicatechin, epigallocatechin, epicatechin gallate, epigallocatechin gallate, gallocatechin gallate	bactericidal effects on oral bacteria, <i>Aggregatibacter actinomycetemcomitans</i>	Chang et al., 2019
epicatechin epicatechin gallate epigallocatechin epigallocatechin gallate	antioxidant	Grzesik et al., 2018
catechin	antioxidant, anti-inflammatory, beneficial effect in the management of diabetic autonomic neuropathy in rats	Addepalli V et Suryavanshi SV, 2018
catechin	antibacterial	Gomes et al., 2018
catechin	antioxidant	Caro et al., 2019
catechin	hepatoprotective	Akinmoladum et al., 2018
catechin	cytotoxic	Di Leo et al., 2017
catechin	anti-microbial	Chunmei et al., 2010
epigallocatechin-3-gallate	antioxidant,	Roychoudhur et al., 2017
epigallocatechin-3-gallate	antibacterial	Founier-Larente et al., 2016
catechin	antioxidant, antibacterial	Akiboye et al., 2016
catechin	antibacterial	Diaz-Gomez et al., 2013
catechin	antibacterial	Diaz-Gomez et al., 2014
catechin	antibacterial antioxidant	Li et al., 2018
catechin	antibacterial	Zhang et al., 2016
catechin	antifungal	Saito et al., 2013s
epigallocatechin gallate	antibacterial	Nakayama et al., 2013

Several authors have highlighted the antibacterial effect of polyphenols against bacteria that can cause gastrointestinal diseases.

Several studies associate catechin with different antibiotics. It has been observed that the combination of antibiotics like catechin-imipenem, catechin-erythromycin, catechin-tetracycline would have a synergistic inhibition effect against *Eschericia coli*, which suggests that polyphenols may be considered promising alternatives for the treatment of bacterial and viral infections, thus the catechin can be used for the prophylaxis of influenza and A (H1N1) infection (Gomes et al., 2018; You et al., 2018; Diaz-Gomez et al., 2013). Other studies demonstrate that black tea consumption would influence the incidence of *Helicobacter pylori* infection due to its catechin content (Boyanova et al., 2015; Naveeda et al., 2018; Diaz-Gomez et al., 2013).

### 8. Antidiabetic effect

Certain studies have pointed out that catechin would have a significant potential to reduce blood glucose, body weight and body mass index (BMI) in both elderly and obese subjects by stimulating thermogenesis (Hashemipour et al., 2017; Pastoriza et al., 2017; Addepalli et al., 2018). Catechins control plasma glucose levels by modulating the glucose transport system (Grzesik et al., 2018).

### 9. Immunostimulatory effect

Catechin also intervenes in immune function modulation through humoral and cellular mechanisms. It has been emphasized that catechin decreases cyclophosphamide-induced myelosuppression (Ganeshpurkar et al., 2018).

## Conclusions

Catechin and its derivatives represent a class of phenolic compounds with a very wide therapeutic potential. At present, not all the mechanisms of action are fully known, but studies have shown that these compounds would be worthwhile investigating.

Numerous studies have shown positive effects of green tea and tea-based products due to their content of catechin and its derivatives. These compounds would also be beneficial for the improvement of degenerative, metabolic and cardiovascular diseases as well as the quality of life in elderly population. Studies on cell lines highlight the effects of catechin on cancer chemopreventive activity. However, catechins and their derivatives must be given full attention due to numerous effects, for the development of new, more efficient and more stable drug structures. There are currently no food supplements with catechin or its derivatives in pure form, but most of the green tea extract supplements are based on its effects and its derivatives.

## Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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