

Acacia Catechu Willd. for CRC

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The research for innovative treatments against colon adenocarcinomas is still a great challenge. *Acacia catechu* Willd. heartwood extract (AC) has health-promoting qualities, especially at gastrointestinal level. This study characterized AC for its catechins content and investigates the apoptotic-enhancing effect in human colorectal adenocarcinoma HT-29 cells, along with its ability to spare healthy tissue. Results showed that AC induced an increase in apoptotic cells and ROS formation, reduction in mitochondria membrane potential as well as increase in caspase-9 and -3 activity. AC did not affect rat ileum and colon rings viability and functionality, suggesting its safe profile toward healthy tissue. The present findings outline the potential of AC for colon cancer treatment.

Keywords: *Acacia Catechu* Willd. ; colorectal cancer ; apoptosis ; HT-29 cells ; ROS ; mitochondria membrane potential ; catechins ; polyphenols ; natural compounds

1. Introduction

Colorectal cancer (CRC) is one of the most common causes of tumour deaths worldwide ^[1]. In Europe, it is the second and the third most common form of cancer for women and men, respectively. Its occurrence and progression depend on multiple issues, among which family, age, gender and personal history constitute the major risk factors ^[2]. Standard treatments include surgery and chemotherapy. In the latter case, drugs induce DNA damage or initiate multiple signalling pathways, including cell cycle arrest, DNA repair, etc., leading to cancer cell death. The outcome of chemotherapeutic drugs in patients, however, is related to the cancer subtype, and often the effects of cytotoxicity, drug resistance and adverse reactions constitute overwhelming problems ^[3].

Natural products continue to provide leads for compounds endowed with pharmacological activities, especially those for treating many types of cancer ^[4]. A recent report highlighted that 49% of the small molecules approved in the area of cancer from the 1940s to 2014 were natural products or novel structures directly derived from them ^[5]. These compounds have cytotoxic properties owing to many different mechanisms of action, such as the inhibition of tumour cell growth accompanied by the induction of apoptosis, DNA damage, etc. Furthermore, anticancer drugs have greater potential to kill tumour cells if administered in combination with plant-derived compounds, and hopefully have less adverse effects. To explore this possibility, several clinical trials for various cancers were performed, including those for CRC ^[6].

2. *Acacia catechu* Willd.

Acacia catechu Willd. extracts have been used in traditional medicine for the treatment of several diseases. It possesses hepatoprotective, antipyretic, antidiarrheal, hypoglycaemic, anti-inflammatory, immunomodulatory, antinociceptive, antimicrobial, free radical scavenging and antioxidant activities ^{[7][8][9][10]}. Moreover, recent studies have demonstrated that *Acacia catechu* Willd. exerts spasmolytic and antispastic activities in vitro by interacting with calcium channels and muscarinic receptors, without affecting *Lactobacilli* and *Bifidobacteria*, the most represented intestinal species, suggesting that it may benefit patients suffering from diarrhoea ^[11]. *Acacia catechu* Willd. extract contains high amounts of flavonoids, such as flavan-3-ols, (+)-catechin, (–)-epicatechin, (–)-epicatechin-3-O-gallate and (–)-epigallocatechin-3-O-gallate ^[12]. These derivatives and related polyphenols possess apoptosis-inducing activity in several cancer cell lines ^[13]. Thus, this study investigates the effects of a preparation obtained by *Acacia catechu* Willd. heartwood by decoction (AC) on human colorectal adenocarcinoma HT-29 cell line in order to highlight its potential use in cancer therapy. As the capability of AC to spare the viability and functionality of normal tissue may be of clinical interest, this aspect was also investigated in rat ileum and colon rings. The results showed that AC has potential as an anti-cancer agent, as it exhibits irreversible anti-proliferative effects and induces intrinsic apoptosis, while sparing healthy tissue.

The present study outlines the potential of AC for CRC treatment, as this extract induced cytotoxicity of human colorectal adenocarcinoma HT-29 cells, which was accompanied by increases in apoptotic cells and ROS formation; a reduction in MMP; and increases in caspase-9 and 3 activities. AC did not affect rat ileum and colon rings viability and functionality,

suggesting a safe profile toward healthy tissue. Moreover, AC main components are absorbed rapidly and eliminated slowly [14], and this might constitute an added value to the potential use of AC for CRC prevention.

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