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Review Article

Phytochemical, Nutritional and Pharmacological Potentialities of Carob (*Ceratonia siliqua* L.,): A Review

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Abstract

Carob tree *(Ceratonia siliqua L.)* belongs to the leguminosae family and it is manly cultivated in Mediterranean regions. It is well accepted by the people for its nutritional, pharmacological, phytochemical and therapeutic functions in the human body. Seeds and pulp of *Ceratonia siliqua* are eaten by humans or to animals, which contain carbohydrates, fibers, polyphenol, minerals and many other phytochemicals. This review aims to represent the nutritional and pharmacological activities of *Ceratonia siliqua* L. To have a better understanding, we have discussed the nutritional status of *Ceratonia siliqua* L., its available phytochemicals and their functional properties. The availability of various important phytochemicals along with their functional properties makes *Ceratonia siliqua* L. valuable for pharmaceuticals and industry.

Keywords: *Ceratonia siliqua* L.; Pharmacological; Phytochemicals

Introduction

Ceratonia siliqua L. is an endemic, aromatic and medicinal plant which is found to be currently among the most successful forest fruit and fodder trees that exist in the Morocco (Say, 2008). It is a xerophytic tree shoving some special characteristics such as hardiness, resistance to drought, soil fertilization and the fight against soil erosion. It has been exploited for a very long time, in particular thanks to its qualities fodder and food. Thanks to its biological and ecological peculiarity, it has been included in the national list of priority as a forest resource for conservation. Indeed, it is an agro-sylvopastoral species that can be used for the rehabilitation for degraded soils, thanks to its capacity adaptation to different edophoclimatic conditions (Say, 2008). This evergreen tree presents very high economic profitability compared to other fruit species. In Morocco, it covers an area exceeding 30000ha, more than half of which is in the domain forestry, which favors a very important national production of carob pods (AitChitt et *al.,* 2007).

The carob tree has, in addition, a great socio-economic interest since its pods, more rich in sugars than sugar cane and sugar beet, and which are used in industry food and pharmacological (Batlle and Tous, 1997; Gharnit et *al.,* 2001). Carob is a essential reservoir of nutritional and pharmaceutical compounds. More specifically the locust bean seeds are generally used for the production of locust bean gum. All the parts of this tree are useful and exploited for their great wealth and their added value in several areas. The leaves are a popular fodder and have dietetic and medicinal properties. In addition, the bark and leaves were used in the traditional medicine as a laxative, diuretic, antidiarrheal and for the treatment of gastroenteritis (El Bouzdoudi et *al.,* 2017). These leaf extracts contain multiple medicinal properties: cytotoxic and antimicrobial (Meziani et *al.,* 2015; Meziou-Chebouti et *al.,* 2015), antioxidants (Custodio et *al.,* 2011; Rtibi et *al.,* 2016) and antifungals (Fadel et *al.,* 2011); Inhibitors of proliferation of tumor cells (Corsi et *al.,* 2002; Custodio et *al.,* 2011) andhepatoprotective (Ibrahim et *al.,* 2012).

The present review aims to summarize and discuss the nutritional and phytochemicals and pharmacology of this useful and unexploited part of carob tree.

Phytochemicals

The carob pods has high amounts of carbohydrates (40-60%), polyphenolic compounds especially tannins (18-20%), dietary fibers (27-50%) (Marakis, 1996), minerals (potassium, sodium, iron, copper manganese and zinc) (Karki et *al.,* 2007; Gulay et *al.,* 2012)and low amounts of protein (3-4%) and lipids (0.4-0.8%) (Biner et *al.,* 2007; Özcan et *al.*, 2007; Vekiari et *al.,* 2011). This fruit is known especially, for its richness in sugars which are essentially composed of sucrose (32-38%), fructose (5-7%) and glucose (5-6%) (Rtibi et al., 2017), but their relative proportions are variable (Marakis, 1996). The pods also contain a high amount of dietary fiber and phenolic compounds (Avallone et *al.,* 1997). There are many date about the chromatography methods performed by HPLC (High-Performance Liquid Chromatography) for determining polyphenols in carob pods which revealed the presence of condensed tannins (proanthocyanidins), had flavan(3-ol groups and their galloyl esters, gallic acid, (+)-catechin, epicatechingallate and quercetin glycosides (Ghenemi et *al.,* 2017; Custodio et *al.,* 2011; Corsi et *al.,* 2002; Ortega et *al.,* 2009) and several authors referred also to the presence ofhydrolysable tannins (Gallotannins and ellagitannins) in carob pods (Avallone et *al.,* 1997) .It had polyphenols astannins, flavonoids (26%) and phenolic acids (such as gallic acid, cinnamic acid and p-coumaric acid), favone glycosides (such asquercetin-3-a-L-rhamnopyronoside) and hydroxytyrosol (Owen et *al.,* 2003). In addition, the carob juice is rich in electrolytes such potassium, sodium iron, copper, manganese and zinc. The chemical substance in carob pods differ widely according to carob species, climate and the stage if maturity as well as to different parts of tree. Indeed, the HPLC analysis was showed that the principal compounds are: pyrogallol (3.55%), catechin (19.10%) and tannic acid (9.01%) in mature carob pods. However, this technique revealed the pyrogallol (48.02%), catechin (16.52%), gallic acid (15.12%),

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chlorogenic acid 15.01%) and epicatechin (12.26%) in immature carob pods (Rtibi et *al.*,2016). In addition, this technique detected many phenolic compounds in leaves as kaemferol (77%), tannin acid (13%) catechin hydrate (4.30%) and polydatin (0.85%). Likewise, it was found that carob tree leaves are richer in fiber than the carob pod. However, the carob extract is richer in total and reduced sugars compared to leaves (El Bouzdoudi et *al.,* 2017; Ghanemi et *al.,* 2017, Owen et *al.,* 2003; Rtibi et *al.,* 2015; Rtibi et *al.,* 2016).

Biological Activities

Recently, it has been reported that the tree studied as having multiple biological activities, especially in digestive tract including antioxidant, antidiarrheal, antibacterial, anti-ulcer, anticancer, anti-carcinogenic, anti-mutagenic and anti-inflammatory actions (Yamagishi et *al.,* 2000; Greenspan et *al.*, 2005; Lambert et *al.,* 2005; Moreno et *al.,* 2006; Song et *al.*, 2007).

Antioxidant Activity

Methanol extracts of the leaves and pulps (all sexes of the tree) were tested for radical scavenging (DPPH) and antioxidant (carotene-linoleate) activities and leaves extract found to be more active (El Hajjaji et *al.,* 2010; Roseiro et *al.*,2013; Saoud et *al.*,2019; Ashande et *al.*,2019 et Oscar et *al.,* 2020).

Anti-inflammatory and Related Activities

Methanol extract of bark was tested for antioxidant (DPPH), acute toxicity (rats) and chemical (Carrageenan) or mechanical poworedema. It was analyzed for major compound families and flavonoids, tannins, sterols, quinones and mucilages were found. A galactomannan extracted from pods, authors refer to as Locust bean gum was used as constrast material in magnetic resonance enteroclysis (MRE) for imaging of Crohn's disease (bowels chronic inflammatory disease). It gave best results when used with water and mannitol. Leaves were extracted with dichloromethane: methanol 1:1v/v. The extract was tested for anti-inflammatory and cytotoxic activities and found inactive in both (Rtibi et *al.,* 2017).

Anti-Diabetic Effect

Ethanol/water (96%) extract of dry pods was tested for streptozotocin-induced diabetes in rats. It decreased blood glucose and lipids. Mixture of dried flowers of Roselle (Hibicussabdariffa) and dry pods of Carob was water extracted and administered to alloxan-induced diabetic rats. The extract was tested with or without Gamma radiation of the plants mixture powder. In both cases it was found active. Phenolic compounds may also have antioxidant effect used for managing oxidation stress-related chronic diseases such as diabetes and hypertension (Rtibi et *al.,* 2018; Custodio et *al.,* 2015).

Anti-Obesity Effect

Obesity is undeniably one of the biggest medical problems of the 21st century due to dietary habit, sedentary lifestyle, and stress, which promotes various cardiovascular disease and pathologica conditions like hypertension, inflammation, and hepatosteaosis (Kuzbicka and Rachon, 2013).

Antimicrobial, Antifungal, Antiviral and Related Activities

Methanolic extract of *Ceratonia siliqua* was tested for antibacterial activity, compared with methanolicextrct of Plantago major, which was found more active for most bacteria. The extract of *Ceratonia siliqua* was more active of *Escherichia coli*, *Staphyococcusaureus (*Kivçak et *al.,* 2002), the carob would also adsorb enterotoxins produced by certain strains of *Esherichia coli* and *Staphylococcusaureus* as well as by the chera *Vibrio*, and thisadosprtion mechanism could be explained by the presence of tannins in the insoluble and active part of the carob. In addition to his power nematicide demonstrated by the work of El Allagui et *al.,* (2007) which is due to its content of compounds phenolic, according to a recent study by Sanchez et *al.*,2010 the carob tree is a good source carbohydrate market for bioethanol production. Aqueous and methanolic extract were tested of antimicrobial activity, alone and in combination with other antibacterial agent (ampicillin, gentamicin, amikacin and clindamycin). The combination of extracts and antibacterial agents was more efficient than each separately. The extracts were analyzed and some pure compounds were isolated and characterized. Ethanolicand acetone extracts was tested of antibacterial activity against *P. atrosepticum* in Potato soft rot. Acetone extract was more active. Methanolic extract of leaves found to be active against Listeria moncytogenes. HPLC analysis of extracts yielded seven compounds with antibacterial activity, especially epigallocatechin-3-gallate. However, antifungal activity with ethyl-acetate and methanol has been observed against *Condida albicans. The MICs of the aqueous extract of Ceratonia siliqua* varied between 30 mg/ml for *Staphylococcusaureus* and 50 mg/ml for E. coli and *Condida albicans* (Singh et *al.,* 2016; Al-Seeni, 2017, Aissani et *al.,* 2012, Kivçak et *al.,* 2002; Hsouna et *al.,* 2015; Aissani et *al.,* 2012).

Newcastle Disease, caused by Newcastle Disease Virus (NDV), is a serious threat to the global poultry industry due to its high mortality rate (Alexander, 2000). Ethanolic extract of *Ceratonia siliqua* leaves was tested against NDV and found partially active. The gradual concentrations of carob leaves extract (500, 240 and 50µg/ml) showed 20, 40 and 80% mortality, respectively (Al-Hadid, 2016). These findings demonstrate a dose dependent manner of plant extract and mortality. Nevertheless, total inhibition of viral activity was not observed, suggesting the need to increase concentrations of the plant extract (Azab, 2017).

Anticancer Activity

Ethanolic and ethyl acetate extracts of propolis that was collected in an area (Morocco) with Carob as a major tree were prepared, and tested against three mammalian tumor cell lines Medium activity was measured. Dry pods were extracted with ethanol, and it was analyzed for reductive components (very detailed), antioxidant, and anti-cancer and antical pain activities. It was found moderately active for the three activities. Aqueous extracts of dry pods or leaves were tested against mouse hepatocellular carcinoma cell line, and both found active, but leaves extract was more active. Authors attribute this activity to the presence of gallic acid and some of its esters. Methanolic extracts of pods and leaves were prepared and tested for anti-proliferative and apoptotic activities in MDA-MB-231 human breast cancer cells, and found active, with higher activity of leaves extract. Authors relate these activities to the presence of phenolic compounds (Ghanemi et *al.*,2017).

Other Usages

Several studies have shown that the use of soils associated with

polyethylene glycol (PEG) improves the digestibility and nutritional quality of the tannins contained in the leaves (Priolo et *al.,* 2000), the latter were used in Turkey, in 'traditional' medicine to treat diarrhea and in the diet and in the treatment of obesity (Berrougui, 2007).The leaves were also referred to as being carries of cytotoxic, antimicrobial, antioxidant and antifungal activities (Kivçak and Mert, 2002; Custodio et *al.,* 2011; Fadel et *al.,* 2011; Meziani et *al.,* 2015; MeziouChebouti et *al.,* 2015).Corsi et *al.*, (2002); Custodio et *al.,* (2011) demonstrated the extraordinary ability leaf and pod extracts to inhibit tumor cell proliferation.

According to some authors, the soluble fibers of the pulp can have a preventive or curative effect on human and animal health, thanks to the reduction of the risk of thrombosis through the decrease in blood pressure and serum cholesterol level (Williams et *al.,* 1995; Beagger et *al.,* 1996; Konate, 2007). In therapy, this essence is known for its cholesterol-lowering, antiproliferative, anti-diarrheal effect, and other digestive disorders, laxative and nourishing (Berrougui, 2007). In addition, it plays an effective role in the suppression of intestinal parasites (Min and Hart, 2003) and in the treatment of diarrhea (Serairi-Béji et *al.,* 2000).

From research has shown that carob may be a good candidate for use as a functional food or as a food ingredient (Tsatsaragkou et *al.,* 2014; Biernacka et *al.,* 2017; Arribas et *al.,* 2019; Salih and Jilal, 2020) because it can constitute a good source of antioxidant polyphenols (Owen et *al.,* 2003).

Numerous clinical studies have highlighted the effectiveness of carob powder in the treatment of acute childhood diarrhea (Serairi-Béji et *al.,* 2000), which was confirmed by the study clinic conducted by Loeb et *al.,* (1989). The pulp is recommended against tuberculosis pulmonary and bronchial diseases. In decoction, however, it is antidiarrhoeal and slightly purifying. It is used for the treatment of certain diseases such as gastritis, enteritis, tonsillitis, colds, cancer… (Crosi et *al.,* 2002).

Conclusion

The carob tree may be considered as a valuable plant in both traditional and modern drugs development areas for its medicinal uses. Standardization of carob pods and extracts leaves extracts can be carried out for direct use against various above mentioned problems and further research can be undertaken for isolation, purification and pharmacological validation of active constituents responsible for particular pharmacological activity.

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