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Ceratonia siliqua L. A Promising Functional Food for Chronicle Diseases Related to Gastrointestinal System: Diabetes, and Lactose Intolerance †

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Abstract: The present study contributes to the promotion of a tree widely cultivated in the Mediterranean area, especially in our country Algeria; the carob tree "*Ceratonia siliqua* L."; by a bibliographic mini review which lists the chemical, nutritional, biochemical, biological, and biotechnological properties of carob and its by-products expressed by the evaluation of its activities: antioxidant, anticancer, anti-hyper-lipidemic, anti-diabetic, anti-reflux, anti- diarrheal, antibacterial, anti-inflammatory, antiulcer and enzymatic, noted in the literature for few years. The presence of the main primary and secondary metabolites: polyphenols, fibers and sugars; give these products very interesting properties and benefits for human health by making it dietetic product and a raw material of choice in food, pharmaceutical and biotechnology industries, in this perspective we developed in our laboratory a *Ceratonia siliqua* L. fruit aqueous extract based vegetal milk as a functional food for chronicle diseases related to digestive disorder: diabetes, and lactose intolerance.

Keywords: Mediterranean local products; *Ceratonia siliqua* L.; carob; functional food; nutraceuticals

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1. Introduction

Ceratonia siliqua L. belongs to legumes' family, it is widly cultivated in Mediterranean region, where it is considered as a natural component of biodiversity and a famous local product, used by local population since ancient times for alimentation as well as traditional remedy. According to FAOSTAT 2019 statistics it is cultivated on 80,000 hectares for a world production of 160,000 t/year, with varying production yields depending on cultivars, soils, climates and agri-parctices. It is also beneficial to the local agricultural economy since it is a drought- and temperature-tolerant plant [1,2].

Last decades, scientific researches focus on tree parts application especially biological and biotechnological ones [3,11], as its bioactive components could be very interesting for functional foods industry, food supplements, nutraceuticals..., mostly because it is usually conceded as by-products.

In this context, the present mini review aims to promote renewable local bioresouces for an agriculture based on responsible and sustainable Eco-economy.

2. Experiments

Intensive and rigors researches using several national and international references (articles, books, reviews in Electronic databases: MDPI, Science Direct, Springer, ACS, RS, Pub Med, Pub Chem., Google Scholar...) were performed since 1981 until our days, to study evolution of scientific research on *Ceratonia siliqua* L. in time, and how it performs in regard of varying fields: ethnobotany, ethnopharmacology, Chemistry, Nutrition, Biological and Biotechnogical applications in order to extract maximum informations concerning investigated plant.

3. Results and Discussion

According to our review, scientific researches are generally increasing for example we identified 872 Articles for 2000 and 620 Articles for 2010, highlighting by the way growing interest, currency and relevance of studied plant. Obtained results, lead to enumerate achievements and lacks which could be interesting to investigate in the future.

3.1. Origin and Geographic Distribution

De Candolle (1883) and Vavilov (1951) reported carob tree origin to Turkey and Syria region, while Schweinfurth (1894) reported it to Yemen region. Nowadays it is extended around Mediterranean region from Spain and Morocco to Turkey [12,13], and is introduced in many other countries: USA, Australia, Argentina, India... [14].

It is grow in holm oak stand in association with *Olea europea* et *Pistacia lentiscus* [15], and is restant to salent poor soils, and sub-arid climate [16,19] which make it a natural green fence against soils degradation, erosion and desertification [18,20].

3.2. Current Uses

3.2.1. Traditional Use

Several ethnopharmalogical surveys reported carob tree among most cited plants by herbalist and local informant for nutritional value and treating gastro-intestinal system diseases [21,24].

3.2.2. Food Industry

Carob pod pulp is used as cattle feed in addition to barley floor [25,26].

Carob flour obtained by grinding terrified dried pods after shelled, is widely used in dietary food industry due to its high content in sugars, free gluten and phenols which is recommended for oeucolic persons [17,27–28], it is also used in preparation of milk flour [29–31], drinks, citric acid, jams, sirup, honey [13,15,32] as substitute of cacao in chocolate and biscuits [29].

Seeds tires is used as substitute of pectin, gelatin, stabilizer, fixer in several products such as cheese, sauces, mayonnaise; it is also used as thickening E410 in candy production [33].

3.2.3. Cosmetology

Due to its capacity to form viscous solutions at low concentrations, its thinking, emulsifier and stabilizing proprieties [14,34,35]; it is used as natural adjuvant in soaps, creams, toothpaste... [36].

3.3. Chemical Composition

3.3.1. Primary Metabolits

- Carob tires

Major constituent of carob tires is a galactomannane (80–85%), a polysaccharide present in carob seeds [37], in addition to 13% of lipids; 4% of proteines, 1–4% of celluloses and lignin and 1% of ashes and water content [38].

- Pod pulp

Pod pulp is rich in simple hydrocarbs (saccharose, fructose, glucose) and fibers [39,40] and its content depends on culyivars, soils, seasons and climates. [14,41–44]. Algerian cultivars reports 37.5 to 45.3% total sugars content, and according to Avallone (1997)

[45], the average composition is 27–40% of Saccharose, 3–5% of Glucose, 3–8% of Fructose, 2–6% of Protéines, 0.4–0.6% of Lipids, 2–3% of ashes and 27–50% of Fibers.

3.3.2. Secondry Metabolits

- *Phenols*

Carob is an interesting phenols source (16–20%) [45,46], with a high molecular weight even in comparison with other plants [47], responsible of its antioxidant activity [48,49].

According to Owen (2003), flavones content in carob is about 0.132 g/kg) [42], Würsch (1984) and Saura-Calixto (1988) reported a tannin content of 16–20% on dry weight in pods [47,50].

Kamal K. et al. (2013), reported that coumarins content in carob flour is about 4,49ppm while lignins are about 33.06 ppm [51].

3.4. Nutritional Value

Carob fruit is relatively caloric sice 100 g of caroub flour give about 222 kcal/933 kJ [51].

3.5. Biological Activities

3.5.1. Antioxydant Activity

Several phytochemical studies were realized using DPPH and ABTS tests showing an important antioxidant activity [17,49,52–53].

3.5.2. Aticancer Activity

Polyphenols and fibers are offently reported as cancer inhibitors especially colorectal one which is negatively correlated to a rich fiber diet [54]. Consequently, carob fibers are potent agents in cancers prevention [55].

3.5.3. Antihyper Lipidic Activity

According to Valero-Munoz (2014–2017) studies, carob fibers are active in the treatment of blood lipid troubles due to the high quantity of insoluble fibers: cellulose and hemicelluloses and/or polyphenols in carob fibers [57].

Carob gum as soluble fiber has the potent to lower plasmatic blood cholesterol value [57]. Moreover, Carob fibers hypocholesterol agent derivative was patented [58].

3.5.4. Antidiabetic Activity

In vitro studies reported Carob gum as a blood glicemian reductor [59].

3.5.5. Antireflux Activity

Prior studies, reported Carob gob as infants reflux reductor and its symptoms [60–62].

3.5.6. Antidiarrehal and Antibacterial Activity

Kivçak, et al. (2002) found positive results for *Ceratonia siliqua* L. leaves inhibitory effect on different *Escherichia coli strains, Staphylococcus aureus and Staphylococcus epidermidis,* thus, glyconutriments in Carob act as prébiotiques, which make it a diarrhea natural treatment [49,63].

5. Conclusions

The present bibliographic mini review on carob tree and its organic derivatives (pods, pulp, seeds, flowers, leaves), exhibits its richness in several primary (fibers, hydrocarbs) and secondary metabolites (phenols, Gallic acids, catechins, quercetin, tannins...) which content and profile depend on plant studied part, soil, climate, cultivar, extraction and characterization methods. Besides, an important antioxidant activity, a high nutritional value and dietary profile make its plant parts derivatives very interesting functional foods, dietary supplements, adjuvant in pharmaceutics, nutraceutical, to treat several chronically diseases related to nutrition such as cancer, diabetes, ulcer, gluten intolerance.

In this regard, a range of dietary products was developed in our laboratory: free gluten floor, molasses, vegetable milk, tires, to promote local organic products for a sustainable eco-responsible economy.

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References

1. Essahibi, A.; Benhiba, L.; Babram, M.A.; Ghoulam, C.; Qaddoury, A. Influence of arbuscular mycorrhizal fungi on the functional mechanisms associated with drought tolerance in carob (*Ceratonia siliqua* L.). *Trees* **2018**, *32*, 87–97.
2. Boutasknit, A.; Baslam, M.; Ait-El-Mokhtar, M.; Anli, M.; Ben-Laouane, R.; Douira, A.; El Modafar, C.; Mitsui, T.; Wahbi, S.; Meddich, A. Arbuscular Mycorrhizal Fungi Mediate Drought Tolerance and Recovery in Two Contrasting Carob (*Ceratonia siliqua* L.) Ecotypes by Regulating Stomatal, Water Relations, and (In) Organic Adjustments. *Plants* **2020**, *9*, 80, doi:10.3390/plants9010080
3. Ben Ayache, S.; Behija Saafi, E.; Emhemmed, F.; Flamini, G.; Achour, L.; Muller, C.D. Biological Activities of Aqueous Extracts from Carob Plant (*Ceratonia siliqua* L.) by Antioxidant, Analgesic and Proapoptotic Properties Evaluation. *Molecules* **2020**, *25*, 3120, doi:10.3390/molecules25143120
4. Custódio, L.; Fernandes, E.; Escapa, A.L.; López-Avilés, S.; Fajardo, A.; Aligué, R.; Albericio, F.; Romano, A.Antioxidant activity andin vitroinhibition of tumor cell growth by leaf extracts from the carob tree (*Ceratonia siliqua*). *Pharm. Boil.* **2009**, *47*, 721–728.
5. Meziani, S.; Oomah, B.D.; Zaidi, F.; Simon-Levert, A.; Bertrand, C.; Zaidi-Yahiaoui, R. Antibacterial activityof carob (*Ceratonia siliqua* L.) extracts against phytopathogenic bacteria Pectobacterium atrosepticum. *Microb. Pathog.* **2015**, *78*, 95–102.
6. Rtibi, K.; Selmi, S.; Grami, D.; Amri, M.; Eto, B.; El-Benna, J.; Sebai, H.; Marzouki, L. Chemical constituents and pharmacological actions of carob pods and leaves (*Ceratonia siliqua* L.) on the gastrointestinal tract: A review. *Biomed. Pharmacother*. **2017**, *93*, 522–528.
7. Klenow, S.; Jahns, F.; Pool-Zobel, B.L.; Glei, M. Does an Extract of Carob (*Ceratonia siliqua* L.) Have Chemopreventive Potential Related To Oxidative Stress and Drug Metabolism in Human Colon Cells? *J. Agric. Food Chem.* **2009**, *57*, 2999–3004.
8. Kumazawa, S.; Taniguchi, M.; Suzuki, Y.; Shimura, M.; Kwon, M.-S.; Nakayama, T. Antioxidant activity of polyphenols in carob pods. *J. Agric. Food Chem.* **2002**, *50*, 373–377.
9. Dimassi, O.; Rached, M.; Fawaz, R.; Akiki, R. Polarimetry and Spectrophotometry to detect adulteration in commercial carob molasses in Lebanon. *Int. J. Sci. Environ. Technol.* **2019**, *8*, 345–357.
10. Karaca, O.B.; Saydam, I.B.; Güven, M. Physicochemical, mineral and sensory properties of set-type yoghurts produced by addition of grape, mulberry and carob molasses (Pekmez) at di_erent ratios. *Int. J. Dairy Technol.* **2011**, *65*, 111–117.
11. Tounsi, L.; Ghazala, I.; Kechaou, N. Physicochemical and phytochemical properties of Tunisian carob molasses. *J. Food Meas. Charact.* **2019**, *14*, 20–30.
12. Rejeb, M.N. Le caroubier en Tunisie: Situations et perspectives d'amélioration. In *Quel Avenir Pour L'amélioration des Plantes?* AUPELF-UREF, ed.; John Libbey Eurotext: Paris, France, 1995; pp. 79–85.
13. Gharnit, N.; El Mtili, N.; Ennabili, A.; Sayah, F. Importance socio- économique du caroubier (*Ceratonia siliqua* L.) dans la Province de Chefchaouen (nord-ouest du Maroc). *J. Bot. Soc. Bot. France* **2006**, *33*, 43–48.
14. Batlle, I.; Tous, J. *Carob Tree Ceratonia silique L.*; Promoting the conservation and use of underutilized and neglected crops. 17.; Institute of Plant Genetic and Crops Plant Research, Gatersleben/International Plant Resources Institute: Rome, Italy, 1997; pp. 91–97.
15. Rejeb, M.N.; Laffray, D.; Louguet, P. Physiologie du caroubier (*Ceratonia siliqua* L.) en Tunisie. In *Physiologie des Arbres et Arbustes en Zones Arides et Semi-Arides*; Groupe d'Etude de l'Arbre, Paris, France, 1991; pp 417–426.

16. Baum, N. *Arbres et Arbustes de l'Egypte Ancienne*; Edité par Peeters Publishers: Belgium, Germany, 1989; p. 354.
17. Sebai, H.; Souli, A.; Chehimi, L.; Rtibi, K.; Amri, M.; El-Benna, J.; Sakly, M. In vitro and in vivo antioxidant properties of Tunisian carob (*Ceratonia siliqua* L.). *J. Med. Plant Res.* **2013**, *7*, 85–90.
18. Zouhair, O. *Le Caroubier: Situation Actuelle et Perspectives D'avenir, Document Interne, Eaux et Forêts, Maroc*; Centre de Recherche Forestière: Rabat, Maroc, 1996; p. 22.
19. Gil-Albert, F. *Tratado de Arboricultura Frutal, La Ecología del Árbol Frutal*, 4th ed.; Pesca y Alimentación, Ediciones Mundi-Prensa; Ministerio De Agricultura: 1998, Volume II, 205 p.
20. Correia, P.J.; Gama, F.; Pestana, M.; Martins-Loução, M.A. Tolerance of young (*Ceratonia siliqua* L.) carob rootstock to NaCl. *Agric. Water Manag.* **2010**, *97*, 910–916.
21. Ouelbani Rayene; Bensari Souheir; Mouas Toma Nardjes; Khelifi Douadi. Ethnobotanical investigations on plants used in folk medicine in the regions of Constantine and Mila (North-East of Algeria). *J. Ethnopharmacol.* **2016**, *194*, 196–218, doi:10.1016/j.jep.2016.08.016.
22. Merzouki, A.; Ed-derfoufi, F.; Molero Mesa, J. Contribution to the knowledge of Rifian traditional medicine. II: Folk medicine in Ksar Lakbir district (NW Morocco). *J. Fitoter.* **2000**, *71*, 278–307.
23. Benitez, G.; Gonzalez Tejero, M.R.; Molero-Mesa, J. Pharmaceutical ethnobotany in the western part of Granada province (Southern Spain): Ethnopharmacological synthesis. *J. Ethnopharmacol.* **2010**, *129*, 87–105.
24. Gonzalez-Tejero, M.R.; Casares-Porcel, M.; S'anchez-Rojas, C.P.; Ramiro-Guti´errez, J.M. Medicinal plants in the Mediterranean area: Synthesis of the results of the project Rubia. *J. Ethnopharmacol.* **2008**, *116*, 341–357.
25. Chitt, A.; Belmir, M.; Lazrak, M. Production des plantes sélectionnées et gréffées du caroubier. In *Transfert de Technologie en Agriculture: N° 153*; IAV Rabat: Rabat, Maroc, 2007; pp. 1–4.
26. Louca, A.; Papas, A. The effect of different proportions of carob pod meal in the diet on the performance of calves and goats. *Anim. Prod* **1973**, *17*, 139–146.
27. Sahle, M.; Coleon, J.; Haas, C. Carob pod (*Ceratoniasiliqua*) meal in geese diets. *Brit. Poultry Sci.* **1992**, *33*, 531–541.
28. Berrougui, H. Le caroubier (*Ceratonia siliqua* L.), une richesse nationale aux vertus médicinales. *Maghreb Can. Express* **2007**, *5*, 9.
29. Yousif, A.K.; Alghzawi, H.M. Processing and characterization of carob powder. *Food Chem.* **2000**, *69*, 283–287.
30. Makris. D.P.; Kefalas. P. Carob Pod as a source of polyphenolic Antioxidants. *Food Technol. Biotechnol*. **2004**, *42*, 105–108.
31. Dakia, P.A.; Wathel, B.; Paquot, M. Isolation and chemical evaluation of, carob (*Ceratoniasiliqua* L.*)* seed germ. *Food Chem.* **2007**, *102*, 1368–1374.
32. Bonnier, G. *La Grande Flore en Couleurs (Tome 3)*; Edité par Belin: Paris, France, 1990; pp.309–310.
33. Ndir, B.; Lognay, G.; Wathelet, B.; Cornelius, C.; Marlier, M.; Thonart, P. Composition chimique du nététu, condiment alimentaire produit par fermentation des graines du caroubier africain Parkia biglobosa (Jacq.) Benth. *Biotechnol. Agron. Soc. Environ.* **2000**, *4*, 101–105.
34. Multon, J.L. *Additifs et Auxiliaires de Fabrication Dans les Industries Agroalimentaires*; Lavoisier: Paris, France, 1984.
35. Goycoola, F.M.; Morris, E.R.; Gidley, M.J. Viscosity of galactomannans at alkaline and neutral pH: evidence of "hyperentanglement" in solution. *Carbohydr. Polym.* **1995**, *27*, 69–71.
36. Calixto, F.S.; Canellas, J. Components of nutritional interest in carob pods Ceratonia siliqua. *J. Sci. Food Agric.* **1982**, *33*, 1319–1323.
37. Kök, M.; Hill, S.; Mitchell, J. Viscosity of galactomannans during high temperature processing: influence of degradation and solubilisation. *Food Hydrocoll.* **1999**, *13*, 535–542
38. Lopez da Silva, J.; Gonçalves, M. Studies on a purifcation method for locust bean gum by precipitation with isopropanol. *Food Hydrocoll.* **1990**, *4*, 277–287.
39. Papagiannopoulos, M.; Wollseifen, H.R.; Mellenthin, A.; Haber, B.; Galensa, R. Identification and quantification of polyphenols in carob fruits (*Ceratonia siliqua* L.) and derived products by HPLC-UV-ESI/ MSn, *J. Agric. Food Chem.* **2004**, *52*, 3784–3791.
40. Makris. D.P.; Kefalas. P. Carob Pod as a source of polyphenolic Antioxidants. *Food Technol. Biotechnol*. **2004**, *42*, 105–108.
41. Biner, B.; Gubbuk, H.; Karhan, M.; Aksu, M.; Pekmezci, M. Sugar profiles of the pods of cultivated and wild types of carob bean (*Ceratonia siliqua* L.) in Turkey. *Food Chem.* **2007**, *100*, 1453–1455, doi:10.1016/j. foodchem.2005.11.037.
42. Owen RW, Haubner R, Hull WE, Erben G, Spiegelhalder B, Bartsch H, Haber B Isolation and structure elucidation of the major individual polyphenols in carob fibre. *Food Chem. Toxicol.* **2003**, *41*, 1727–1738, doi:10.1016/ S0278-6915(03)00200-X
43. Davis, W.L.P.; Orphanos, I.; Papaontantino, J. Chemical composition of developing carob pod. *J. Sci. Food Agic* **1971**, *22*, 83–86.
44. Orphanos, P.I.; Papaconstantinou, J. *The carob varieties of Cyprus. Tech. Bull.5*; Cyprus Agricultural Research Institute, Ministry of Agriculture and Natural Resource: Nicosia, Cyprus, 1969.
45. Avallone, R.; Plessi, M.; Baraldi, M.; Monzani, A. Determination of chemical Composition of Carob (Ceratonia siliqua): Protein, Fat, Carbohydrates, and tannins. *J. Food Compos. Anal.* **1997**, *10*, 166–172, doi:10.1006/jfca.1997.0528.
46. Dewick, P.M. The Biosynthesis of Shikimate Metabolites. *Natural Product Reports* **1995**, *12*, 579–607.
47. Wursch, P.; Vedovo, S.; Rosset, J.; Smiley, M. The tannins granules from ripe carob pod. *Lebensm. Wiss. Technol.* **1984**, *17*, 351–354.
48. Hariri, A.; Ouis, N.; Sahnouni, F.; Bouhadi, D. mise en oeuvre de la fermentation de certains ferments lactiques dans des milieux a base des extraits de caroube. *Rev. Microbiol. Ind. San. Environ.* **2009**, 37–55.
49. El Hajaji, H.E.; Lachkar, N.; Alaoui, K.; Cherrah, Y.; Farah, A.; Ennabili, A.; Lachkar, M. Antioxidant properties and total phenolic content of three varieties of carob tree leaves from morocco. *Rec. Nat. Prod.* **2010**, *4*, 193–204.

50. El Hajaji, H.E.; Lachkar, N.; Alaoui, K.; Cherrah, Y.; Farah, A.; Ennabili, A.; Lachkar, M. Antioxidant activity, phytochemical screening, and total phenolic content of extracts from three genders of carob tree barks growing in Morocco. *Arab. J. Chem.* **2011**, *4*, 321–324.
51. Saura-Calixto, F. Effect of condensed tannins in the analysis of dietary fiber in carob pods. *J. Food Sci.* **1988**, *53*, 1769–1771, doi:10.1111/j.1365-2621.1988.tb07838.x
52. Kamal, M.; Youssef, E.; Moshera, M.; El-Manfaloty, H.; Ali, M. Assessment of Proximate Chemical Composition, Nutritional Status, Fatty Acid Composition and Phenolic Compounds of Carob (*Ceratonia Siliqua* L.). *Food Public Health* **2013**, *3*, 304–308.
53. Colombo, M.L.; Pinorini-Godly, M.T.; Conti, A. Botany and pharmacognosy of the cacao tree. In *Chocolate and Health*; Conti, A., Paoletti, R., Poli, A., Visioli, F., Eds.; Springer: Milan, Italy, 2012; pp 41–62.
54. Rtibi. K. , M.A.; Jabri, S.; Selmi, H.; Sebai, J.C.; Marie, M.; Amri, L.; Marzouki, J. El- Benna, Preventive effect of carob (*Ceratonia siliqua* L.) in dextran sulfate sodium-induced ulcerative colitis in rat. *RSC Adv*. **2016**, *6*, 19992–20000.
55. Kaïs, R.; Slimen, S.; Dhekra, G.; Mohamed, A.; Bruno, E.; Jamel, El.; Hichem, S.; Lamjed, M. Chemical constituents and pharmacological actions of carob pods and leaves (*Ceratonia siliqua* L.) on the gastrointestinal tract: A review. *Biomedicine& Pharmacotherapy* **2017**, *93*, 522–528, doi:10.1016/j.biopha.2017.06.088
56. Keefe, S.J.D. Diet, microorganisms and their metabolites, and colon cancer. *Nat Rev Gastroenterol Hepatol.* **2016**, *13*, 691–706.
57. Johns, L.E.; Houlston, R.S. A systematic review and meta-analysis of familial colorectal cancer risk. *Am. J. Gastroenterol.* **2001**, *96*, 2992–3003.
58. Valero-Munoz, M.; Martin-Fernandez, B.; Ballesteros, S.; Lahera, V.; de las Heras, N. Carob pod insoluble fiber exerts anti-atherosclerotic effects in rabbits through sirtuin-1 and peroxisome proliferator-activated receptor-gamma coactivator-1alpha. *J. Nutr.* **2014**, *144*, 1378–1384.
59. Valero-Muñoz, M.; Ballesteros, S.; Ruiz-Roso, B.; Pérez-Olleros, L.; Martín-Fernández, B.; Lahera, V.; de Las Heras, N. Supplementation with an insoluble fiber obtained from carob pod (*Ceratonia siliqua* L.) rich in polyphenols prevents dyslipidemia in rabbits through SIRT1/PGC-1alpha pathway. *Eur. J. Nutr.* **2017**, *58*, 357–366.
60. Evans, A.J.; Hood, R.L.; Oakenfull, D.G.; Sidhu, G.S. Relationship between structure and function of dietary fibre: A comparative study of the effects of three galactomannans on cholesterol metabolism in the rat. *Br. J. Nutr.* **1992**, *68*, 217–229.
61. Haber, B.; Meer, H.T.; Hausmanns, S. Cholesterol-Reducing Agent Made of Dietary Fibre and Cholesterol Reducing Substances. WO Patent, WO2004009093A1, 29 January 2006.
62. Forestieri, A.M.; Galati, E.M.; Trovato, A.; Tumino, G. Effects of guar and carob gums on glucose, insulin and cholesterol plasma levels in the rat. *Phytother Res.* **2010**, *3*, 14.
63. Miyazawa, R.; Tomomasa, T.; Kaneko, H.; Morikawa, A. Effect of locust bean gum in anti-regurgitant milk on the regurgitation in uncomplicated gastroesophageal reflux. *J. Pediatr. Gastroenterol. Nutr.* **2004**, *38*, 479–483.
64. Miyazawa, R.; Tomomasa, T.; Kaneko, H.; Arakawa, H.; Morikawa, A. Effect of formula thickened with reduced concentration of locust bean gum on gastroesophageal reflux. *Acta Paediatr.* **2007**, *96*, 910–914.
65. Miyazawa, R.; Tomomasa, T.; Kaneko, H.; Morikawa, A. Effect of formula thickened with locust bean gum on gastric emptying in infants. *J. Paediatr. Child Health* **2006**, *42*, 808.
66. Orenstein, S.R.; Magill, H.L.; Brooks, P. Thickening of infant feedings for therapy of gastroesophageal reflux. *J. Pediatr.* **1987**, *110*, 181–186.
67. Georgieva, M.; Manios, Y.; Rasheva, N.; Pancheva, R.; Dimitrova, E.; Schaafsma, A. Effects of carob-bean gum thickened formulas on infants' reflux and tolerance indices.*World J. Clin. Pediatr.* **2016**, *5*, 118–127.
68. Kivcak, B.; Mert, T. Antimicrobial and cytotoxic activities of *Ceratonia siliqua* L. extracts. *Turk J. Biol.* **2002**, *26*, 197–200.