Acta Scientific NUTRITIONAL HEALTH (ISSN:2582-1423)

Volume 6 Issue 8 August 2022

Systematic Review

Kombucha Application in Health: Systematic Review

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DOI: 10.31080/ASNH.2022.06.1093

Received: June 23, 2022

Published: July 11, 2022

Abstract

The kombucha beverage (KB) is a drink resulting from the fermentation of sweetened teas or juices containing a symbiotic consortium of bacteria and yeast as inoculum, also known as Scooby. KB consumption has become popular worldwide due to its various claims and some scientifically established properties including anti-diabetic, hepatoprotective and antioxidant potential, and its effects in metabolic disorders, atherosclerosis, inflammatory problems, arthritis, and cancer. Thus, KB have been studied in animal models to better comprehend its possible effects on human health. Given the above, the present study aimed to systematically review the literature in order to establish in which human health conditions have KB been applied considering animal models. A search was carried out in PubMed, Scopus, Scielo, ScienceDirect, and ISI Web of Knowledge, using the descriptors "(Kombucha [MeSH])" and "(Kombucha tea [MeSH])". Of the 1214 studies found, 40 were included in the systematic review. A total of 24 human health conditions have been investigated considering the use of KB using as experimental research animal models. The health conditions: diabetes, hepatotoxicity and physiological conditions were the most prevalently studied. In conclusion, KB has been studied in diverse human health conditions considering animal models, showing a great potential to modulate biological parameters in both physiological and pathological conditions.

Keywords: Kombucha Beverage; Human Health; Animal Model; Physiological Condition; Pathological Condition

Abbreviations

KB: Kombucha Beverage; SCOBY: Symbiotic Bacteria and Yeast Colony

Introduction

Kombucha beverage (KB) is a traditional drink commonly consumed in Asia [1], and according to its etymology, it is derived from two Japanese words "kombu" for algae and "cha" for tea [2]. The origin of KB is uncertain, but it is believed to have emerged in Manchuria (northeastern China), where it was sought for its suspected "magical" properties [3]. KB is prepared by fermenting sweetened tea using yeast and bacteria as inoculum, a mature bacterial cellulose biofilm also known as tea fungus or SCOBY ("Symbiotic Bacteria and Yeast Colony") [1]. The SCOBY from a previously brewed kombucha culture, is commonly placed over the solution and allowed to ferment for several days. The carbon source in the solution, generally sucrose, is important to initiate a cascade of metabolic processes that generates a carbonated and slightly acidic drink at the end [4].

KB is a combination of three fermentations: alcoholic, lactic and acetic, due to the presence of several coexisting yeasts and bacteria in the environment, being initiated by osmotolerant microorganisms and finally dominated by acid tolerant species [5]. The beverage consumption has become quite popular worldwide due to its various claims and some scientifically established properties including anti-diabetic [6], hepatoprotective [7] and antioxidant potential [6,7], and its effects in metabolic disorders, atherosclerosis, inflammatory problems, arthritis, and cancer [8]. KB is also known for its antimicrobial activity against different pathogenic organisms [1,8-10].

Considering the increasing concern over the alarming rates of diseases worldwide and in light of the promising opportunities of KB regarding prevention and/or treatment of pathological conditions, the present study aimed to systematically review the literature in order to establish in which human health conditions have KB been applied considering animal models.

Materials and Methods

Review question

In which human health conditions have KB been applied considering animal models?

Inclusion and exclusion criteria

The inclusion criterion was studies that used animal models to investigated KB applied to human health outcomes. The use of animal models was conducted to control confounding factors in variables of interest.

The exclusion criteria were studies unrelated to KB, studies related to KB but unrelated to health areas, reviews, congress summaries, patent descriptions, book section, hypothesis articles, commentaries, opinion articles, previews, articles published in different languages than Portuguese, English and Spanish, letters, articles that were not fully available even after attempting to contact the authors.

Search strategy

The electronic search was conducted without initial date restriction up to and including July 2019 in PubMed, Scopus, Scielo, ScienceDirect, and ISI Web of Knowledge databases. The initial search was conducted using the MeSH and relevant entry terms: (Kombucha) OR (Kombucha tea). All references were managed in the EndNote X7 software (Thomson Reuters, New York, NY, US). Initially, duplicate references were excluded. Titles, abstracts, and study methodologies were screened based on the inclusion and exclusion criteria by two independent reviewers (GDS and CCdoA). Lists were compared and in case of disagreement, a consensus was reached by discussion. When a consensus was not achieved, a third reviewer decided if the article should be included (FN). This systematic review followed the PRISMA statements, with some adjustments [11].

Results and Discussion

The initial search yielded 1214 articles. After removing 430 duplicated titles, a total of 784 articles were included for title and abstract screening, remaining 54 articles. After reading the full text 14 studies were excluded and 40 articles remained, satisfying the inclusion criteria. Figure 1 displays the PRISMA flowchart for the study selection process.

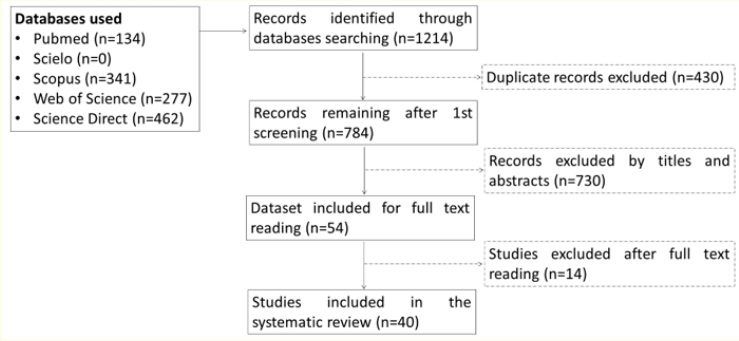

Figure 1: Flowchart of study selection.

Table 1 reports the 24 human health conditions studied by the 40 included articles. The health conditions more prevalent were diabetes (7 studies, 17.5%), hepatotoxicity (6 studies, 15.0%) and physiological conditions (4 studies, 10.0%). Three health conditions (hypercholesterolemia, non-alcoholic fatty liver disease, and myocardial injury) were each evaluated by two studies (5.0%), and eighteen (ulcer, skin wounds, silicosis, hyperglycemia, nephrotoxicity, electromagnetic field exposition, steatosis, irradiation, transient cerebral ischemia and reperfusion, non-alcoholic steatohepatitis, post-operative peritoneal adhesion formation, autoimmune encephalomyelitis in model of multiple sclerosis, aging-related skin abnormalities, oxidative stress, cancer, hyperuricemia, cytotoxicity, and kampuchea-synthesized bacterial cellulose biocompatibility with sciatic nerve) were verified by only one study (2.5%).

Author, year	Animal (sex)	Injury induction	Target	Condition	KB preparation				KB application	
					Tea or juice	Tea or juice concentration*	Sugar concentration*	Fermentation period	Exposure period	Route/ method of administration
Abshenas., *et al*. 2012	Balb/c mice (male)	Acetaminophen by oral administration	Liver	Hepatotoxicity	Black tea	12 g/L	100 g/L	12 days	7 days	Oral/-
Al-Dulaimi., *et al*. 2018	Wistar rats (male)	-	Blood	Physiological[#]	Black tea	1.5 g/L	50 g/L	-	21 days	Oral/Gavage
Aloulou., *et al*. 2012	Wistar rats (male)	Alloxan by intraperitoneal injection + glucose solution after 6 hours	Pancreas	Diabetes	Black tea	12 g/L	100 g/L	12 days	1 month	Oral/Gavage
Banerjee., *et al*. 2010	Swiss mice (male)	Indomethacin dissolved in distilled water and suspended in gum acacia	Stomach	Ulcer	Black tea	5 gl/L	100 g/L	2 - 4 – 7 days	7 days	Oral/-
Barati., *et al*. 2013	Wister rats (male and female)	Open wound created on dorsal surface	Skin	Skin wounds	Black tea	12 g/L	100 g/L	8 - 10 days	20 days	Topical/ Bandage
Bellassoued., *et al*. 2015	Wistar rats (male)	Cholesterol-rich diet	Liver Kidney	Hypercholesterolemia	Green tea	12 g/L	100 g/L	12 days	16 weeks	Oral/ Gavage
Bhattacharya., *et al*. 2013	Swiss rats (male)	Alloxan by intraperitoneal injection	Liver Kidney Pancreas Heart Blood	Diabetes	Black tea	5 g/L	100 g/L	14 days	14 days	Oral/-
Fu., *et al*. 2013	Sprague-Dawley rats (Male and female)	Intratracheal injection of mycillin containing silica dust	Lung	Silicosis	Chinese herbal extract[†]	9 g/L	-	2 weeks	4 weeks	Inhalation /Spray

Gamboa-Gomez., *et al.* 2017	C57BL/ 6 mice (female)	High saturated fat and fructose diet	Blood	Hyperglicemia	Quercus convallata and Quercus arizonica infusions	10 g/L	10 g/L	7 days	14 weeks	Oral/ Gavage
Garib, 2009	Albino rats (male)	Trichloroethylene by oral administration	Kidney Blood	Nephrotoxicity	Black tea	12 g/L	100 g/L	8 - 10 days	2 weeks	Oral/-
Gharib., *et al.* 2014	Wistar rats (male)	Exposed to microwave 950 MHz	Brain Spleen Intestine	Electro magnetic field exposition	Black tea	12 g/L	100 g/L	-	1 week	Oral/ Stomach tube
Hartmann., *et al.* 2000)	C57-BL/6 mice (male and female)	-	Brain Heart Kidney Liver Spleen	Physiological[#]	Black tea	2.5 g/L	70 g/L	7 days	-	-
Hosseini., *et al.* 2015	Wistar rats (male)	Single intraperitoneally injection of 120mg/kg alloxan BW	-	Diabetes	Green tea	12 g/L		-	4 weeks	Oral/Gavage
Hyun., *et al.* 2016	C57BLKS and C57BLKS db/db mice (male)	Methionine/ choline-deficient diet	Liver	Steatosis	Black tea	10 g/L	100 g/L	14 days	3 weeks	Oral/-
Ibrahim, 2011	Albino rats (male)	Cadmium chloride by intraperitoneal injection + Gama irradiation of whole body	Liver Kidney Blood	Irradiation effects	Black tea	12 g/L	100 g/L	8 - 10 days	2 weeks before treatment + 4 weeks after treatment	Oral/Gavage
Jayabalan., *et al.* 2010	Albino rats (male)	Aflatoxin B1 by intraperitoneal injection	Liver	Hepatotoxicity	Black tea	12 g/L	100 g/L	14 days	30 days	Oral/ Drinkers
Jung., *et al.* 2019	C57BLKS db/db mice (male)	Methionine/ choline-deficient diet	Liver	Non-alcoholic fatty liver disease (NAFLD)	Black tea	10 g/L	100 g/L	14 days	3 weeks	Oral/-
Kabiri., *et al.* 2013	Wistar rats (male)	Thioacetamide by intraperitoneal injection	Liver Blood	Hepatotoxicity	-			-	3 weeks	-
Kabiri., *et al.* 2014	Wistar rats (male)	Thioacetamide by intraperitoneal injection	Liver	Hepatotoxicity	Black tea	12 g/L	100 g/L	12 days	3 weeks	-
Kabiri and Setorkim, 2016	Wistar rats (male)	Middle cerebral artery occlusion	Brain	Transient cerebral ischemia and reperfusion	-	10 g/L	80 g/L	8 - 10 days	-	Intraperitoneal/ Intraperitoneal injection

Lobo and Shenoy, 2014	Wistar rats (male)	Isoproterenol by subcutaneous administration	Heart Blood	Myocardical injury	Black tea	7.5 g/L	100 g/L	7 days	30 days	Oral/-
Lobo., *et al*. 2017	Wistar rats (male)	Isoproterenol by subcutaneous administration	Heart Blood	Myocardical injury	Black tea	7.5 g/L	100 g/L	7 days	30 days	Oral/-
Lee., *et al*. 2019	C57BKS db/db mice (male)	Methionine/ choline-deficient diet	Liver Blood	Non-alcoholic fatty liver disease (NAFLD) Non-alcoholic steatohepatitis (NASH)	Black tea	10 g/L	100 g/L	14 days	4 weeks	Oral/-
Maghsoudi and Mohammadi, 2009	Wistar rats (male)	Abdominal operation	Abdomen	Post-operative intraperitoneal adhesion formation	-			-	-	Intrape ritoneal/-
Marzban., *et al*. 2015	C57BL/6 mice (female)	Inoculation of myelin oligodendrocyte glycoprotein-35-55 by injecting subcutaneously + 2 doses of lyophilized pertussis toxin by intraperitoneal injection	Brain Cere bellum Heart Blood	Autoimmune encephalo myelitis in model of multiple sclerosis	Black tea	12 g/L	100 g/L	12 days	3 weeks	Oral/-
Murugesan., *et al*. 2009	Albino rats (male)	Carbon tetrachloride by Intraperitoneal injection of	Liver Blood	Hepatotoxicity	Black tea	10.5 g/L	100 g/L	14 days	30 days	Oral/-
Pakravan., *et al*. 2018	NMRI mice (female)	-	Skin	Aging-related skin abnormalities[#]	Black tea	12 g/L	100 g/L	14 days	14 days	Intra dermal /-
Sai Ram., *et al*. 2000	Sprague-Dawley rats (male)	Force feeding of sodium dichromate	Liver Blood Eryth rocyte	Oxidative stress	Black tea[‡]	12 g/L	100 g/L	8 - 10 days	-	Oral/ Gastric cannula
Salarfzoon., *et al*. 2018	BALB/c mice (female)	Invasive breast cancer cell subcutaneously injected into the left flank	Tumor Blood Liver Kidney	Cancer	Ginger tea	-	100 g/L	10 days	30 and 60 days	Oral/ Gavage
Semjonovs., *et al*. 2014	Wistar rats (male)	High-fat diet	Blood	Physiological[#]	Black tea	12 g/L	70 g/L	1 day	60 days	Oral/ Intragastric tube
Srihari., *et al*. 2013	Wistar rats (male)	Streptozotocin by intraperitoneal injection	Blood Liver	Diabetes	Black tea[‡]	4.5 g/L	100 g/L	14 days	45 days	Oral/ Stomach tube
Sukrama, 2015	Wistar rats	High purine diet	Blood	Hyperuricemia	-			4 - 8 - 12 days	-	-

Vijaya raghavan., *et al*. 2000	Wister rats (female)	-	Blood Lung Liver Spleen Kidney Heart	Physiological[#]	Black tea[‡]	10 g/L	100g/L	8 days	90 days	Oral/Gavage and drinkers
Wang., *et al*. 2014	ICR mice (male)	-	Liver Blood	-	Black tea	5 g/L	100 g/L	8 days	35 days	Oral/Intra gastrically
		Acetami nophen by intra peritoneally injection	Liver Blood	Hepatotoxicity	Black tea	5 g/L	100 g/L	8 days	2 weeks	Oral/Intra gastrically
Yang., *et al*. 2009	ICR mice	Hyperchole strolaemic diet	Liver	Hyperchole sterolemia	Black tea	5 g/L	100 g/L	8 days	12 weeks	Oral/-
Yapar., *et al*. 2010	Albino mice (male)	Phenol	Erythro-cyte Lung Liver Heart Stomach Intestine Kidney	Induced cytotoxicity	Black tea	20 g/L	200 g/L	8-10 days	20 days	Oral/Gavage
Zhu., *et al*. 2014	Sprague-Dawley rats (male)	Sciatic nerve exposition by making a skin incision and splitting the underlying muscles in the left lateral thigh	Sciatic nerve	Kampuchea-synthesized bacterial cellulose biocomp atibility with sciatic nerve	Black tea	5 g/L	100 g/L	7 days	1 - 3 - 6 weeks	Surgical/ Surgically implan tation into the spatium inter musculare along the sciatic nerve.
Zubaidah., *et al*. 2018	Wistar rats (male)	Streptozotocin by intraperitoneal injection	Pancreas Blood	Diabetes	Snake fruit juice	1000 g/L	100 g/L	14 days	28 days	Oral/-
Zubaidah., *et al*. 2019a	Wistar rats (male)	Streptozotocin by intraperitoneal injection	Pancreas Blood	Diabetes	Snake fruit juice	20 g/L	100 g/L	14 days	28 days	Oral/-
					Black tea	20 g/L	100 g/L	14 days	28 days	Oral/-
Zubaidah., *et al*. 2019b	Wistar rats (male)	Streptozotocin by intraperitoneal injection	Pancreas Blood	Diabetes	Snake fruit juice	1000 g/L	100 g/L	14 days	28 days	Oral/Intra gastrically tube

Table 1: Description of animal characteristics, substance, conditions and dose used to induce health conditions, and the main methodology used for KB preparation and treatment of induction by author and year of publication.

* Values present in the included articles and standardized for this review.

Without induction of pathological condition.

† Mixing tea (2 g/L) + dried *Siratia grosvenori* fruit (5 g/L) + wild chrysanthemum (2 g/L).

‡ Black tea described by the article as industrialized brand.

The literature is not clear as to what led to the initial research in these three health conditions (diabetes, hepatotoxicity and physiological conditions). It can be speculated that since KB is a popular beverage included among many traditional fermented foods across the world and its consumption has been related long ago to curative effects on a number of human diseases, mainly based on personal observation and testimonials could have contributed to the onset of studies in the animal models related to diabetes, hepatotoxicity, and physiological conditions.

Diabetes is one of the most prevalent diseases in the world, with an estimated 693 million people affected in 2045 [12]. Its complications involve increased cardiovascular risk, including atherosclerosis, nephropathy, retinopathy, and neuropathy [13]. In this context, KB has been studied for its hypoglycemic and antilipemic effects [14]. In studies with diabetic rats, the KB reduced the levels of pancreatic amylase and lipase, leading to a reduction in cholesterol, triglycerides, and serum glucose [6,14].

In addition, treatment with KB decreased glycated hemoglobin [6,15] a parameter that assesses the glycemic average of the last 3 months in humans. Finally, KB was able to reduce the oxidative stress caused by hyperglycemia [6,16], as well as having a preventive effect against kidney injuries by reducing urea and creatinine and liver injuries by reducing alkaline phosphatase (ALP) and alanine transaminase (ALT) [6]. These results show the therapeutic and preventive potential of KB in the face of diabetes and its complications, thus stimulating increased research in this area.

The liver is responsible for metabolizing most of the drugs and toxins present in the body and, therefore, any damage caused by hepatotoxic agents has serious consequences. In both prophylaxis and treatment, KB was able to reduce levels of bilirubin, lactate dehydrogenase (LDH), gamma-glutamyl transpeptidase (GGT), ALT, ALP, and aspartate aminotransferase (AST) [17-20], enzymes that can indicate liver damage when they are increased. It also reduced the amount of malondialdehyde (MDA), a marker of oxidative stress [17,18]. Histologically, the results also demonstrated that KB has a hepatoprotective effect [17-19], that is, it can protect the liver against injuries. Thus, it is possible that KB can be used to modulate biological parameters in liver damage and/or used as a hepatoprotective agent in situations of predisposition to liver damage.

Studies were also carried out to evaluate the effects of KB in a physiological environment, that is, without special diets or toxicity induction. A decrease in ALT, AST and ALP was observed, which, as already mentioned, are markers of liver damage, in addition to a reduction in cholesterol, low-density lipoprotein (LDL) and triglycerides, responsible for the development of atherosclerosis [21,22]. In addition, it reduced serum glucose, preventing the onset of diabetes, as well as increased levels of high-density lipoprotein (HDL), which prevents the formation of atherosclerosis [21]. The animals that received KB showed weight gain, in addition to an increase in liver and splenic weight, but they had a longer life span and increased behaviors indicative of increased environmental awareness and responsiveness [23]. Through histology, no organ toxicity was observed, and there was no development of addiction to drinking [24]. On the other hand, KB demonstrated cytotoxicity against thymocytes, perhaps be attributed to the alcoholic content of the drink (about 1.5%) [24].

In all other applications of KB - gastric ulcer, hypercholesterolemia, silicosis, nephrotoxicity, electromagnetic field exposition, hepatic steatosis, irradiation effects, non-alcoholic fatty liver disease, transient cerebral ischemia and reperfusion, myocardial injury, post-operative intraperitoneal adhesion formation, autoimmune encephalopathy in multiple sclerosis, aging-related skin abnormalities, oxidative stress, breast cancer, hyperuricemia, induced cytotoxicity and biocompatibility with sciatic nerve - benefits were attributed to the consumption of the drink [25-42].

Studies used mostly male rodents (30 studies, 75.0%), 5 used females (12.5%), 3 used both genders (7.5%) and 2 did not report this variable (5.0%). The condition induction was most commonly accomplished through chemical substance administration (23 studies, 57.5%) and diet consumption (8 studies, 20%).

Among the tea used to develop the KB, the black tea (30 studies, 75.0%) and green tea (2 studies, 5%) were the most prevalent, 4 articles did not inform the tea used (10.0%).

The effects of KB can be attributed to its chemical composition. The antibacterial and antioxidant effects can be related to the pres-

ence of acetic acid, capable of combating bacterias such as *Helicobacter pylori* - associated with gastritis, peptic ulcer and even gastric cancer [10,43] and to bind to toxins and eliminate them from the body [28]. In addition to acetic acid, there are several other components with antioxidant properties, such as gluconic acid, glucuronic acid, polyphenols, and flavonols [6,19], which may be responsible for the hepatoprotective effect and reduction in the lipid profile [18,21]. Polyphenols, such as theaflavins and thearubigins, can also prevent the damage and death of pancreatic cells, one of the kombucha's antihyperglycemic mechanisms [15,28]. Moreover, the drink seems to have a direct insulinotropic effect on the pancreas, that is, it induces the release of insulin, in addition to decreasing gluconeogenesis [15]. Organic acids (mainly acetic, gluconic, glucuronic acid, citric, L-lactic, malic, tartaric, malonic, oxalic, succinic, pyruvic, and usnic); sugars (sucrose, glucose and fructose), water-soluble vitamins, amino acids, biogenic amines, purines, pigments, lipids, proteins, hydrolytic enzymes, ethanol, carbon dioxide, polyphenols, minerals (manganese, iron, nickel, copper, zinc, plumb, cobalt, chromium, and mcadmium), anions (fluoride, chloride, bromide, iodide, nitrate, phosphate, and sulfate), D-saccharic acid-1,4-lactone, and metabolic products of yeasts and bacteria, are also found in the drink composition [44], and could contribute for its biological effects.

Although KB preparation can vary, it is usually made with black tea [45,46], in agreement with our results. This preference can be due to higher concentrations of ethanol, lactic acid, gluconic acid, and acetic acid, obtained with black tea in comparison to other substrates. Green tea, which is also widely used for KB production, has advantages over black tea, such as reduced fermentation time. However, the oxidation of black tea leaves has a unique flavor [10,47], which may be another reason for the greater use of this tea.

The KB needs to be sweetened so that the fungi and bacteria colonies can grow, producing an adequate fermentation [45]. Although most antioxidant activities increase with incubation time, prolonged fermentation is not recommended due to the high concentration of organic acids, which can be harmful for human and animal consumption [48]. In addition, the CO_2 generated can accumulate at the interface between the biofilm and the broth, blocking nutrients exchange and creating a starvation environment [48].

Thus, It has been described as an adequate fermentation time of approximately 15 days, however, the choice of the fermentation period also depends on the expected sensory attributes of KB consumers [46].

In regard to the KB fermentation period, 17.5% (7 studies) used ≤ 7 days, 25% (10 studies) ranged from 8 to 10 days, 42.5% (17 studies) used ≥ 11 days, 2.5% (1 study) used 4, 8 and 12 days and 12.5% (5 studies) did not inform the period used.

The animal exposure to KB was up to 3 weeks in 37.5% of the studies (15 studies), from 4 to 6 weeks in 35.0% (14 studies), more than 6 weeks in 15% (6 studies) and not mentioned in 12.5% (5 studies) of the studies included in the systematic review.

There was great variation in the period of animal exposure to KB, ranging from 7 days to 16 weeks [19,26]. Indeed, there is a lack of consensus on the ideal period of animal exposure to KB. This could be attributed in part to the different health conditions that have been evaluated (n = 24), as well as the effects expected when treating health conditions with KB, which can vary significantly. Additionally, no study found toxicity in the consumption of KB, generating doubt if the same would occur in longer experiments.

The administration of KB used mostly the oral route (75.0% of the studies) and the intraperitoneal, topical, inhalation, intradermal and surgical route were used in 15.0% of the studies; the remaining studies did not describe the route of KB administration. Gavage (9 studies, 22.5%) is the method predominately used for KB administration when the oral route was chosen, others methods included stomach tube (2 studies, 5.0%), drinkers (2 studies, 5.0%), intragastrically tube (3 studies, 7.5%) gastric cannula (1 study, 2.5%), surgically implantation into the spatium intermusculare along the sciatic nerve (1 study, 2.5%), intraperitoneal injection (1 study, 2.5%), spray (1 study, 2.5%), bandage (1 study, 2.5%) and not informed (20 studies, 50.0%).

Regarding the administration of KB, the oral route through gavage was the most used, possibly due to the greater control of the quantity consumed by the animals. Even so, several methods were used according to the necessity of the experiment, which demonstrates the heterogeneity of the studies presented in this systematic review.

Although KB has several applications in the health field with good results, there is a scarce number of studies in humans [49] and most lack methodology standardization, leading to a great risk of bias. In this sense, experimental research conducted in animal models provides a controlled environment that enables the comprehension of biological mechanisms of physiological and pathological conditions. Yet is important to interpret results with caution when translating experimental results in animal models to humans. However, there is little evidence about harm in terms of drink consumption in humans, with isolated cases and involving a small number of individuals [8].

Conclusion

In conclusion, KB has been studied in 24 human health conditions considering animal models, most commonly in diabetes, hepatotoxicity, and physiological conditions, showing a great potential to modulate biological parameters in both physiological and pathological conditions. Thus, studies are necessary to verify other health conditions that could benefit from KB effects and to comprehend its biological mechanism of action, as well as the conduction of well-designed studies in humans so that these results could sum to the existing knowledge from experimental research in animal models.

Acknowledgements

The authors have no acknowledgements to declare.

Conflict of Interest

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