

POTENTIAL BIOLOGICAL ACTIVITIES OF CRAFT BEER: A REVIEW

ATIVIDADES BIOLÓGICAS DA CERVEJA ARTESANAL: REVISÃO

A.R.
ARTIGO DE REVISÃO

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ABSTRACT

Beer production and consumption have increased, stimulated by the popularity of craft beer. The presence of bioactive compounds in beer is described in the literature, including antioxidants related to benefits to human health. This review discusses, in particular, the potential biological activities of craft beer. Results showed that craft beer could potentially have a beneficial effect on cardiovascular disease, diabetes, cancer, neurological disorders, menopause, osteoporosis and oxidative stress. Also, the addition of new ingredients and production techniques can lead to a beverage with potential health value-added. However, further investigation on the health potential of craft beer is needed.

KEYWORDS

Biological activity, Craft beer, Hops, Malt, Phenolic compounds

RESUMO

A produção e o consumo de cerveja têm aumentado, devido à popularidade da cerveja artesanal. A presença de compostos bioativos na cerveja está descrita na literatura, incluindo de antioxidantes relacionados com benefícios para a saúde humana. Esta revisão tem como objetivo discutir, em particular, as potenciais atividades biológicas da cerveja artesanal. Os resultados mostraram que a cerveja artesanal pode, potencialmente, ter um efeito benéfico nas doenças cardiovasculares, diabetes, cancro, distúrbios neurológicos, menopausa, osteoporose e stress oxidativo. Também, a adição de novos ingredientes e as técnicas de produção podem levar a uma bebida com um maior impacto positivo na saúde. No entanto, continua a ser necessária mais investigação sobre os potenciais benefícios da cerveja artesanal para a saúde.

PALAVRAS-CHAVE

Atividade biológica, Cerveja artesanal, Lúpulo, Malte, Compostos fenólicos

INTRODUCTION

The number of craft breweries has grown every year. In the United States of America (USA), in a universe of 7450 breweries, 7346 were classified as craft breweries. In terms of sales, craft beers grew 4% compared to 2017, representing 13.2% of the total beer market in the USA (1). In Portugal, there are about 640 thousand consumers of craft beer. Portuguese craft beer market has grown five times above the market's mean between 2017 and 2019. In 2017 there were 120 breweries in activity, 115 of which correspond to microbreweries (2, 3). Although industrial beer is still the most common beer, craft beer has been gaining popularity. Craft beer is characterised by production in small and independent breweries, with an annual production of 6 million barrels or less (4). Also, alcohol content must come from beer made with traditional or innovative ingredients and fermented using yeast (5).

Beer has four main ingredients: malted cereals, hops,

water and yeast. The most used cereal is barley. However, wheat, sorghum or rye can also be used. Beer contains several phenolic compounds, which are derived from malt (two-thirds) and hops (one-third), and contribute to beer's flavour, aroma, and chemical stability (6, 7). In general, craft breweries use high-quality raw materials during beer production, which may be related to the presence of different phenolic compounds in craft beers (6,8). Phenolic compounds can act as antioxidants and prevent the oxidative degradation of beers. The mostly reported phenolic compounds in beer include flavonoids, hydroxycoumarins, phenolic acids, tannins, proanthocyanidins, and amino phenolic compounds. All these phenolic compounds have been related to antioxidant activity, as well as other biological effects (6, 9).

The alcohol and nutrients content in beer has a wide variation depending on raw materials and production techniques. The main component of beer is water

(approximately 90%), followed by alcohols resulting from the fermentation process (on average 3.5–10%), carbohydrates (1–6% w/V), and minerals. Beer is also composed of CO₂, inorganic salts, nitrogen, organic acids, higher alcohols, aldehydes, esters, sulphur compounds, hop derivatives and B complex vitamins. Other elements are present but only in small amounts and are known as trace elements (10). One liter of beer can contain 150 to 1100 Kcal, but the average is 143,3 Kcal (11, 12). One liter of beer is responsible for 3 g to 5 g of protein and up to 61 g of carbohydrates (11).

The popularity of craft brewers is due to its focus on organoleptic characteristics, particularly flavour. To achieve these, a careful selection of raw materials (e.g. malt, hops and yeast strains), and changes in manufacturing processes (e.g. in mashing times and temperatures, fermentation and maturation), are made to obtain a product more appealing to the consumer (13,14). However, although craft beers are becoming more popular, most studies related to potential health benefits are still performed with industrial beers. Therefore, this review aims to explore the proven or potential biological activities of craft beer to develop healthier beverages.

METHODOLOGY

For this review, a search was carried out in the databases ScienceDirect, PubMed and Web of Science, using the keywords “Craft Beer”, “Antioxidant Assays”, “Biological Activity”, “Phenolic Compounds”, “Polyphenol”, “Hops”, “Malt” and “Therapeutic Use”. The inclusion criteria were reviews and research papers focusing on studies in craft beer’s biological activity. Preference was given to articles after 2010; however, some articles published between 2000 and 2009 were included because of their relevant information to the topic.

Potential Biological Activities of Craft Beer

Beer is rich in bioactive compounds, with a potential protective role in human health. Diverse physiological effects and health benefits in cardiovascular disease, diabetes, specific cancer types, neurodegenerative diseases and osteoporosis have been associated with low-moderate (up to 1 drink per day in women, up to 2 in men) beer consumption (6, 12, 15).

Cardiovascular Diseases

Moderate and regular consumption of craft beers beverages is associated with cardioprotective effects (12). This effect can be noted in adults, including higher-risk populations (diabetes, hypertension, hypercholesterolemia, heart disease, or overweight and smokers) (16). At low doses, alcohol consumption may lead to an increase in High-Density Lipoproteins (HDL) cholesterol and appears to decrease Low-Density Lipoproteins (LDL) cholesterol (17). Also, it may reduce platelet aggregation, fibrinogen and some procoagulant factors other than fibrinogen (18). The authors found a positive relationship between alcohol consumption and plasminogen activator (19). Brenner et al. (2001) concluded that the inverse relation between alcohol consumption and cardiovascular disease risk was robust among subjects who consumed exclusively or predominantly beer. (20). Increased levels of HDL-cholesterol and positive effect on blood lipid profile were confirmed among moderate beer consumers (21).

Other possible protective mechanisms should be considered, such as specific estrogenic and antioxidant activity or prevention of an alcohol-induced rise in serum homocysteine (20). In addition, the presence of antioxidants in beer may protect the vascular endothelium and prevents LDL oxidation, which is an important step in atherogenesis (19).

Beer compounds showed a protective effect on the cardiovascular system, including ischemic stroke, congestive heart failure, peripheral arteriopathy, and coronary heart disease (12). The beer phenolic content reduced leukocyte adhesion molecules and inflammatory biomarkers (12).

Beer is also a source of folate (20mg per standard drink), vitamin B6 (0,15mg per standard drink) and B12 (0,07mg per standard drink), which are involved in the pathways of homocysteine, a risk factor for cardiovascular disease (12). Therefore, Rossi et al. (2020) evaluated whether craft or industrial beer consumption could reduce serum homocysteine. Although industrial beer reduced homocysteine levels, the consumption of craft beer did not modify this parameter. However, craft beer increased the level of gamma-glutamyl transpeptidase (GGT) (16.6 vs. 18.6 U/L) and reduced the concentration of vitamin B6 (20.9 vs. 16.9 ng/ml). The two types of beer used in the study had different amounts of alcohol (23.8 g in craft beers vs. 11.9 g in industrial beers) which could explain the absence of effect on homocysteine by craft beers. However, it is essential to mention that other parameters can affect homocysteine blood levels like physical activity or diet (22).

Diabetes

Koppes et al. found that the consume of 6–48 g/day of alcohol is associated with 30% of reduced risk of type 2 diabetes, compared with heavier consumers or abstainers (23). Although the mechanisms are not entirely clear, it seems to be related with modulation of changes in the endocrine functioning of fat tissue, modulation of the inflammatory status of several organs, or modulation of metabolism, leading to an increase of insulin sensitivity (24, 25).

Protein glycation, a normal part of the ageing process, has been implicated in various complications of diabetes *mellitus*, and many phenolic compounds are important inhibitors of this process. Since beer is rich in phenolic compounds, Elrod et al. (2017) studied the hypothesis that this beverage inhibits protein glycation. The common craft beer styles studied were American pale ale, porter, stout, India pale ale (IPA), and Imperial IPA. Also, a major, mainstream commercial American beer (American lager style) was purchased for comparison purposes. The study was performed *in vitro*, using bovine serum albumin. Most beers decreased glycation by approximately 30–40%, whereas industrial beer produced an increase in glycation by around 12% over controls. All styles inhibited protein glycation on a volumetric (4 µL/mL) basis, and all but one sample of Imperial IPA inhibited glycation based on phenolics (4 µg of phenols/mL). Thus, different beer styles have extra antioxidant and protein glycation effects, which opens the possibility for craft beer to be designed as a functional beverage, inhibiting protein glycation and potentially preventing the development of complications in type 2 diabetes (26). Since it was an *in vitro* study, further research is needed.

Cancer

Although heavy drinking is related to carcinogenesis (especially to cancers of the mouth, pharynx, larynx, esophagus, and liver), moderate beer drinking seems to have potential cancer-preventive effects (27). Epidemiological and *in vivo* studies in animal models showed a significant decrease in the risk of prostate cancer, renal cell cancer and colorectal tumorigenesis (17, 28). Also, beer components have the potential to modulate carcinogens metabolism, inhibiting its action (27). Hop compounds appear to be the main responsible for the cancer-preventive potential of beer by its apoptosis-inducing, anti-estrogenic, anti-angiogenic, anti-inflammatory, antiproliferative, and antioxidant activities and modulation of carcinogens metabolism (28).

Neurological Disorders

Beer is one of the primary dietary sources of silicon in bioavailable form (silicic acid or orthosilicic acid) (29). Silicon seems to decrease aluminium bioavailability by blocking its uptake through the gastrointestinal tract and by preventing reabsorption. González-Muñoz et al. (2008) showed that the inclusion of silicon in the diet in the form of silicic acid or beer lowered aluminium levels in mice brains by about 40% when compared to the group that received only aluminium nitrate ($p < 0.01$), leading to reduction of harmful effects of increased cerebral peroxidation. Cerebral peroxidation is linked with neurodegenerative diseases development. Also, aluminium appears to play an active role in the pathogenesis of critical neuropathologic lesions in Alzheimer's disease and other related disorders through cross-linking hyperphosphorylated proteins (30–32).

Moderate alcohol consumption (up to 1 drink per day in women, up to 2 in men) may be associated with a reduced risk of dementia and Alzheimer's disease. However, no clear association between a specific type of alcohol beverage and dementia has been established. Furthermore, the existing literature on beer consumption is limited, and reports are unclear on associating beer consumption and dementia (12, 33, 34). Also, due to its alcohol content, regular beer consumption might not be adequate for all populations (e.g. pregnancy, children, people affected by liver diseases) (35).

Menopause and Osteoporosis

Hot flashes, anxiety, insomnia, and osteoporosis are the significant complications often associated with menopause. A prenylated flavanone from hops, 8-prenylnaringenin, is one of the most potent phytoestrogens and can be used to improve symptoms associated with menopause (36). Beer contains high levels of silicon in the form of biologically active orthosilicic acid $[\text{Si}(\text{OH})_4]$. Malted barley provides the primary source of silicon content in beer (37). Sripanyakorn et al. (2004) found that beer contains about 19 mg Si/l, and serum and urinary silicon levels significantly increased following beer ingestion, showing a good bioavailability (29). Comparing with other references, Casey and Bamforth (2010) found higher levels of silicon in beer, which may be due to more samples of craft beers in their study. They also found that although raw materials are richer in silicon, significant amounts are still found in beer (38). Silicon supplementation of postmenopausal women with osteoporosis inhibits bone resorption and increases trabecular bone volume and bone mineral density. Therefore, beer could help stimulate bone formation and/or reduce the postmenopausal loss of bone mass (39). It was found that women who drink beer have greater bone density, maybe due to the synergic effect of a combination of silicon and isoflavonoids (daidzein, genistein, and others) present in beer (39).

Antioxidant Activity

Oxidative stress is involved in the pathology of many diseases, such as atherosclerosis, diabetes, neurodegenerative diseases, ageing and cancer (40). However, studies have shown that beer contributes to inhibiting or delaying oxidative stress by increasing the total antioxidant capacity of plasma (41–43). The high content of bioactive compounds, mainly phenolic compounds, in beer is possible for its high antioxidant activity (18).

A study conducted by Ruiz-Ruiz et al. (2020) evaluated the antioxidant activity of polyphenols extracted from hop provided by a craft brewery. Hop methanolic extract exhibited adequate amounts of Total Phenolic Content (TPC), expressed in g Gallic Acid Equivalents (GAE)/Kg (1.54 g GAE/kg of discarded hop) and flavonoids (0.61 g CE/kg of

discarded hop). Also, the methanolic extract from hop discarded inhibited 4.24% of 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical (44).

Koren et al. (2017) evaluated 40 Hungarian retail beers, including some craft beers, for folic acid content, antioxidant profile and physicochemical parameters. Results showed that higher antioxidant activity observed in dark and craft beers might be due to special malts, like crystal or caramel malts, and other colouring malts used in its production (45).

Bertuzzi et al. (2020) evaluated parameters like TPC and antioxidant capacity in small (SS), and large-scale (LS) brewed beer samples. Comparing SS and LS beers only considering regular beers (the most representative style) significantly higher values for both TPC and antioxidant capacity were found for SS beer ($506.6 \pm 162.3 \text{ mg}_{\text{GAE}}/\text{L}$ for TPC ($p < 0.01$); $1.6 \pm 0.5 \text{ mM Trolox}$ ($p < 0.001$) and $0.54 \pm 0.08 \text{ mol}_{\text{Trolox}}/\text{mol}_{\text{GAE}}$ ($p < 0.01$), for the ABTS assay; $5.4 \pm 1.7 \text{ mM Fe}^{2+}$ ($p < 0.001$) and $1.8 \pm 0.2 \text{ mol}_{\text{Fe}^{2+}}/\text{mol}_{\text{GAE}}$ ($p < 0.01$) for the Ferric Reducing Antioxidant Power (FRAP) assay. These values can be explained by the fact that, in Italy, the legislation bans pasteurisation and microfiltration processes for SS beer (37). Although pasteurisation and microfiltration are common in industrial beers, these processes are avoided in craft beers since they affect their organoleptic characteristics by decreasing polyphenols and other antioxidants from beer (46, 47).

Beer Innovation

Probiotics are microorganisms used as dietary supplements that, in the correct dosage, are potentially beneficial for human health, especially for the intestinal microbial balance (48,49). However, while the health benefits of lactic acid bacteria as probiotics are well known, little data are available on probiotic yeasts in fermented food (50). Therefore, some studies approached the use of yeasts of probiotic species, like *S. cerevisiae var. boulardii*, *Lactobacillus paracasei* and Kefir. In these studies, it was found that beer could be a vehicle for probiotic delivery once they find an adequate number of viable cells in the final product. Furthermore, because viability is crucial for the efficacy of probiotics, craft beer could be more suitable to be produced as probiotic beer than an industrial beer since craft beer is unpasteurised and unfiltered (43, 49–52).

Craft breweries produce classic beer styles and innovative beers brewed with unusual ingredients like fruits, vegetables, and spices, with a particular focus on environmental-friendly ingredients (53).

For example, the use of goji berries, Umbrian legumes, *Parastrephia lucida*, sapa, propolis and olive (*Olea europaea L.*) leaves as beer ingredients have been studied. The incorporation of these ingredients has shown to increase the concentration of bioactive compounds in beer. Ducruet et al. (2017) added whole and ground goji berries (50 g/L) along the brewing process. The addition of goji berries at the beginning of wort boiling allowed the extraction of more phenolic compounds (335 mg GAE/L for the standard amber ale beer vs 623 mg GAE/L for the beer with goji berries) and the production of a beer with 60% to 80% more antioxidant activity and the best sensory characteristics (54).

Luneia et al. (2018) produced and analysed beers with local spelt and barley malt for which lentils and chickling were added. It was found that beers had a high content of TPC (358 mg/L to 636 mg/L), 1.01 and 1.85 mg/L of isoflavones and more than 15% of recommended dietary allowance of magnesium and potassium (55).

Bustos et al. (2019) produced porter beer enriched with *Parastrephia lucida* with four different concentrations (5, 1, 0.5, and 0.1% w/v).

It was observed that TPC values of the four enriched beers (480.16 to 800.64 mg GAE/L) was significantly higher ($p < 0.05$) than the control beer (413.21 mg GAE/L). The increase in bioactive compounds was linear with the increase in plant concentration. Also, the results of antioxidant activity for enriched beers showed increased values (2.17 ± 0.08 to 5.46 ± 0.04 mmol TE/L for FRAP; 1.38 ± 0.03 to 3.34 ± 0.11 mmol TE/L for ABTS; 10.14 ± 0.76 to 30.58 ± 1.20 mmol TE/L for Oxygen Radical Absorbance Capacity (ORAC)), when compared to control (1.88 ± 0.05 mmol TE/L for FRAP; 1.15 ± 0.10 mmol TE/L for ABTS, 7.86 ± 0.14 mmol TE/L for ORAC) (56).

Also, Sanna & Pretti (2015) studied the effect of *sapa*, a cooked must come from wine grapes, and wine barrel ageing in polyphenol content and antioxidant activities of craft beers. The obtained results suggested that storage of beer in wood barrels that contained red wines or the addition of *sapa* from red wine grapes contributed to enhancing TPC in beers and improved free radical scavenging ability and ferric reducing activity. For control beers, TPC ranged from 331.9 to 496.3 mg GAE/L; for beer enriched with *sapa*, the observed values were between 362.8 and 974.9 mg GAE/L and for wine barrel ageing beer 536.0 to 1035.3 mg GAE/L (57).

Ulloa et al. (2017) studied the influence of the addition of propolis ethanolic extract to beer at different concentrations (0.05, 0.15, and 0.25 g/L). Results showed that bioactive compounds, expressed as TPC and total flavonoids compounds, were higher than control. The concentrations of TPC in enriched beers were 253.0 to 306.5 mg GAE/L, whereas the complete flavonoid content (expressed as milligrams of quercetin equivalents (QE) per liter of beer) ranged from 19.6 to 26.9 mg QE/L. For control beer TPC was 242 mg GAE/L and flavonoid content 16.9 mg QE/L. In addition, the concentration of bioactive compounds increased with the concentration of propolis in the ethanolic extract (58). Guglielmotti et al. (2020) studied the contribution of olive leaves as beer ingredients to this beverage's bitterness and antioxidant activity. Thirteen beer samples were produced, adding olive leaves during boiling at different boiling times (60 and 5 minutes before the end of boiling), in various forms (dry crumbled, infusion, and powder) and concentrations (low and high olive leaves-containing beer) sample. The addition of olive leaves highly increased the polyphenol content of beers. High olive leaves-containing beer samples showed significantly higher values ($p \leq 0.05$), between 525.8 and 795.5 mg/L, compared to 228.1 mg/L of reference beer. Polyphenols extraction from leaves was favoured by heat and boiling time (59).

Pereira et al. (2020) studied wheat craft beers brewed with cashew peduncle (*Anacardium occidentale*) and orange peel (*Citrus sinensis*) to evaluate its physicochemical characterisation, antioxidant activity, and sensory analysis. The results showed that formulations containing 10% (m/m) of cashew peduncle possessed a higher increase in TPC (722.3 ± 13.8 and 726.6 ± 2.6 GAE mg/L), in comparison with formulations which contained 5% (m/m) (640.9 ± 58.2 and 652.2 ± 28.7 GAE mg/L) and significantly ($p < 0.05$) higher antioxidant activity (1725.1 ± 24.7 and 1736.9 ± 58.8 μ M/L, respectively)(60). The use of new plant materials and production techniques can increase the concentration of antioxidant compounds in craft beer, obtaining a beverage with potential healthy value-added and improved stability.

CRITICAL ANALYSIS/CONCLUSIONS

Organoleptic characteristics, high-quality raw materials and the image of a less industrialised product contribute to an increase in the consumption of craft beer instead of industrial beer. Many effects of beer compounds on biological systems have received special attention from the scientific community. Bioactive compounds present

in beer, such as phenolic compounds, have antioxidant activity and may reduce cardiovascular disease and cancer risk. However, few studies address the benefits of a final product for human health since literature focuses on the raw materials or industrial beers, with few studies evaluating the biological activities of the craft beers available on the market. The addition of innovative raw materials and improved production techniques give uniqueness and additional value to beer. By improving production techniques, it may be possible to obtain a beer with an appropriate dose of antioxidants and minimum alcohol content. Therefore, understanding the potential uses of bioactive compounds in craft beer and the possible mechanism of action is essential for developing healthier beverages. However, further investigation on the potential health benefits of craft beer is needed. More in vitro studies regarding its possible mechanisms of action, future clinical and in vivo studies concerning the bioavailability, distribution, efficacy, and safety are needed since all compounds present in craft beer might act in synergy. It is essential to clarify that we do not recommend that adult total life-long abstainers begin drinking for health reasons, even in the absence of contraindications. It is also known that, alongside the well-known harmful effects of alcohol abuse, the real impact of moderate consumption is more complex to elucidate.

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