Chapter 4

Health Potential for Beer Brewing Byproducts

Tsai-Hua Kao

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.76126

Abstract

The beer brewing process involves malting, milling, mashing, boiling, cooling, and fermentation. Approximately 20 kg of byproducts are produced for every 100 liters of beer brewed, of which brewer's spent grains (SG), spent hops (SP), and surplus yeasts (SY) account for approximately 85, 5, and 10%, respectively. SG is rich in cellulose, protein, essential amino acids, phenolics and mineral; SP is rich in nitrogen free extract, fiber and protein; SY is rich in proteins and saccharides; where both SP and SY also are rich in prenylflavonoids and hop bitter acids. Although several nutrients or functional components have been found in such beer brewing byproducts, most of these byproducts are used as animal feed and fertilizers since insufficient research has been devoted to the physiological activities for human. To date, only activities of antiobesity and antiproliferation of cancer cells were possessed by SY. Hence, further research is required to clarify the health potential and novel application of these byproducts for environmental protection and other economic activities.

Keywords: beer brewing byproducts, spent grains, spent hops, surplus yeasts, health potential

1. Introduction

Beer is a popular alcoholic drink around the world. Beer is mainly made from sprouted cereals (mostly barley malt) that are fermented with *Saccharomyces* after hops and water have been added. The product, beer, contains natural carbon dioxide and beer yeast and has characteristics including lasting foam, low alcohol content, and richness of nutrients; because of these features, beer is sometimes called "liquid bread."

Although studies have shown that beer contains several functional components, amounts of these functional compounds in beer are diluted since high water content of beer, and the

substantial calorie value and alcoholic content also limit health effects of beer. Conversely, brewing byproducts may contain more functional components during separation procedure. Their further recycling not only achieves waste reduction but also increases their commercial value. This review is aimed at providing detailed information on beer brewing process and the related byproduct generated, as well as the content of functional components in beer brewing byproducts and their health potential.

2. Brewing beer and brewing byproducts

The common beer brewing process contains four major stages: malting, mashing, wort boiling, and fermentation [1]. Related processes and the corresponding byproducts are shown in **Figure 1** [2].

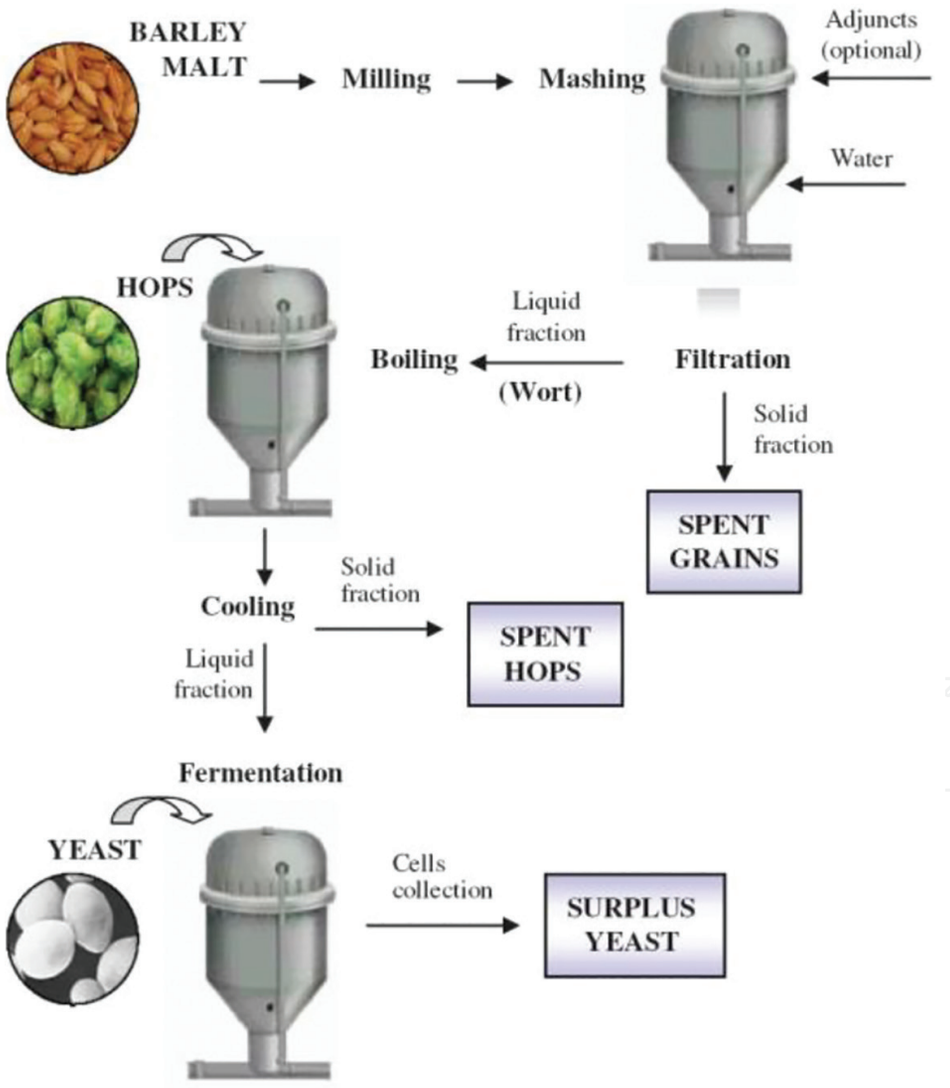


Figure 1. Schematic representation of the brewing process and points where the main byproducts are generated Mussatto [2].

After barley grain has been sieved to remove thinner barley, dust, and impurities, it is steeped in water for germination. During this malting stage, enzymes decompose the complex protein–carbohydrate structure into smaller molecules and expose the starch granules inside the endosperm. Barley grain is allowed to grow only partially because fully grown consumes excessive amounts of starch, and this affects the subsequent fermentation process. Therefore, after the barley grain has germinated, it is dried to halt growth [3].

The malted barley from the malting stage is milled to crush the endosperm completely. Next, the crushed barley is mixed with water and the temperature of the mixture is slowly increased from 37 to 78°C to enhance the hydrolysis capacity of α-amylase and β-amylase. This process converts starch into fermentable sugars (mainly maltose and maltotriose) and unfermentable sugars (maltodextrin), whereas protein is degraded into peptide and amino acids. The process of starch conversion with enzymes is called "mashing". Subsequently, the mixture is filtered; the resultant liquid part is called "wort" and the solid residue is called "spent grains" [4]. During processing, hot water is sometimes added to spent grain to collect second wort. Most beer brews are fermented with a mixture of first and second wort.

During wort boiling step, hops (*Humulus lupulus* L.) are added to the wort, which is then boiled for approximately 1 hour to sterilize the wort and deactivate the glycolysis enzymes. During this process, the components in hops that create a fragrant and the bitter flavor enter the wort and provide the beer with its unique bitter flavor [5]. Moreover, hops enhance beer quality, stabilize bubbles, inhibit glycolysis, and preserve and clarify the wort [6]. After wort boiling has been completed, the wort is filtered again. The solid matter obtained is called "spent hops", which is the second byproduct of the brewing process.

The wort is cooled to between 12 and 18°C for yeast inoculation. Commonly employed yeasts include *Saccharomyces bayanus*, *S. cariocanus*, *S. cerevisiae*, *S. kudriavzevii*, *S. mikatae*, and *S. paradoxus* [1]. During fermentation, the amount of yeast multiplies by three- to six-fold, converting fermentable sugar into ethanol and carbon dioxide; the carbon dioxide is dissolved into the beer. Inoculating different species of yeast gives beer different flavors. The color of beer gradually becomes transparent amber [7]. After the beer aging process has been completed, the yeast cell biomass is collected with all other insoluble materials settled at the tank bottom during filtration. Those insoluble materials are the third brewing byproduct, namely surplus yeasts [1].

3. Composition and current applications of beer brewing byproducts

The beer brewing process produces three byproducts (i.e., spent grains, spent hops, and surplus yeasts. These byproducts remain limited in terms of application and are often used in animal feeds in animal husbandry [2]. The following subsection briefly introduces spent grains, spent hops, and surplus yeasts.

3.1. Spent grains

Spent grains, the most abundant byproduct of beer brewing, accounting for approximately 85% of a brew's total byproduct yield. Spent grains are mainly composed of barley shells, remaining endosperm starch granules, and other cereal additives (e.g., wheat, rice, and corn) added to give beer its unique flavor [1]. The main chemical compositions of spent grains include cellulose, hemicellulose, and lignin. Cellulose and hemicellulose account for 50% of all spent grains. Moreover, spent grains are rich in protein, essential amino acids, minerals, and single sugars (glucose, xylose, and arabinose) [8, 9].

Spent grains are also abundant in phenolics such as ferulic acid, *p*-coumaric acid, syringic acid, vanillic acid and *p*-hydroxybenzoic acid [10]. Mussatto [2] stated that in contrast to that of barley, the composition of spent grains is affected by the following conditions: the barley type, the time of year when barley is planted, the degree to which barley is grinded, and the conditions for malting and glycolysis.

Because spent grains are rich in protein, cellulose, and minerals, they are often used to feed ruminants [11]. Studies have investigated adding spent grains to bread and snacks to increase their fiber content [12]. Spent grains contain many functional groups such as hydroxyl, amine, and carboxyl, all of which can be used as biosorbents. For examples, spent grains can effectively remove volatile substances in exhaust gas and remove contaminants in waste water such as heavy metals (lead, chromium, zinc, copper, and cadmium) and dyes [1, 9, 13]. Moreover, spent grains have proven effective in antioxidation and for antibacterial and anti-inflammatory uses, and can even serve as a precursor for food flavors [14], a medium for producing microbes and enzymes [15], and a raw material for bioethanol [11]. Compared with spent hops and surplus yeasts, spent grains can more easily be reused. In addition, because of the advantages of being high-yielding and containing complex chemical components, spent grain can be used in a variety of areas [4].

3.2. Spent hops

Hops (*Humulus lupulus* L.) are a perennial herbaceous and dioecious plant grown mainly in Europe and North America. The main component of dried hops is fiber, followed by hop bitter acids and protein. Dried hops also contain ash, salts, polyphenols, tannins, and oil [16]. The fiber in hops is composed of xylose, mannose, galactose, and glucose. Of these, glucose and xylose are the most prevalent. In addition, hops contain pectin, uronic acid, rhamnose, and arabinose [17].

Of the added hops, only 15% remain in the final product of beer; the other 85% are residue in spent hops. Therefore, spent hops are abundant in nitrogen-free extract, fiber, and protein [4] and rich in essential amino acids; the composition of spent hops is similar to that of hops [18].

Although spent hops are rich in nitrogen, carbon, and protein, their bitterness limits their application in food. The bitterness of spent hops can be removed with *Candida parapsilosis* fermentation; after this removal, spent hops can be made into animal feed supplements [19]. Because spent hops are rich in nitrogen, they can be used as soil improver and fertilizer.

Spent hops have other applications; for example, oxidized or hydrolyzed spent hops to obtain products with commercial value, including spices, carbohydrates, and organic acids [20]. Furthermore, adding spent hops during the beer brewing process increases yeast activity, which in turn increases the beer yield [21].

3.3. Surplus yeasts

Surplus yeasts are the second most abundant byproduct of beer brewing, accounting for approximately 10% of the total amount of byproducts [1]. After being separated from beer, surplus yeasts are first heated to halt its activity [22]. The composition of *Saccharomyces cerevisiae* determines the composition of surplus yeasts. The major element in yeast is carbon, which accounts for up to 50% of the dry weight, followed by oxygen (30–35%), nitrogen (5%), helium (5%) and phosphorus (1%). Therefore, surplus yeasts are mainly composed of proteins and saccharides [2]. Briggs et al. [5] indicated that because cells vary in terms of their physiological conditions and numbers of bacterial growth cycles, the compositions of different types of surplus yeast also vary.

The protein compositions in surplus yeasts, spent grains, and spent hops are similar in that they all contain several essential amino acids, vitamins, and minerals [2]. The total mineral content in yeast is 5–10% of their dry weight; yeast is especially high in potassium and phosphorus [2].

Chae et al. [23] stated that compared with spent hops, surplus yeast contains more proteins, vitamins, and amino acids, and thus is more often used in animal feeds and nutritional supplements. However, because yeast contains ribonucleic acid (RNA), which is produced by metabolizing uric acid, eating excessive amounts of surplus yeasts can cause gout. Consequently, yeast is limited in the extent to which it can be used in foods [22]. Surplus yeast is often used as a source of carbon and nitrogen when cultivating microorganisms and in health foods in different food seasons [24]. β-glucan, a type of hydrocolloid, can be extracted from surplus yeasts for its ability to improve food characteristics as a thickener, water retaining agent, oil-retaining agent, emulsifier, or foam stabilizer [25]. Parvathi et al. [26] discovered that surplus yeast has the ability to absorb lead.

4. Functional components in beer brewing byproducts

4.1. Dietary fibers

Study revealed that spent grains contained 60–68% of insoluble dietary fibers (IDF) [27]. Another study revealed that dried hops contained 40–50% IDF [16], and beer contained 0.4–6.2 g/L dietary fibers [28]. Lin [29] reported that spent grains contained the most IDFs, followed by hops, spent hops, and surplus yeasts. Spent hops had the highest soluble dietary fibers, followed by spent grains, spent hops, and surplus yeasts. The aforementioned results indicated that during the beer brewing process, dietary fibers in malt and hops were left in spent grains, spent hops, and surplus yeasts, whereas few of them are retained in beer.

4.2. Vitamins

Lewis and Young [30] stated surplus yeasts contained vitamins B1, B2, B3, B5, B6, and B9 in proportions of 15, 7, 50, 10, 3, and 4 mg/100 g, respectively. Bamforth [31] discovered that beer contained vitamin B1 (0.003–0.08 mg/L), B2 (0.02–0.8 mg/L), B3 (3–8 mg/L), B6 (0.07–1.7 mg/L), and B12 (0.003–0.03 mg/L), whereas vitamin E was not detected. However, Lin [29] reported that neither vitamins B, C, nor E were detected in beer brewing byproducts, possibly because the boiling stage in the beer brewing process causes splitting decomposition in vitamins due to high heat and oxidation. Moreover, spent hops and surplus yeast are considered food waste, and thus if brewers do not store them properly, vitamins can be lost.

4.3. Phenolic compounds

Studies have revealed that the sources of phenolic compounds in beer were barley and hops, with barley providing 70–80% and hops providing 20–30% [2]. During the boiling, filtering, and ageing processes, the amount of phenolic compounds changed because phenolic compounds were used to scavenge free radicals and stabilize the flavoring materials and foam in beer [32]. During the cooling process after hops were added, some insoluble materials and polyphenols in the hops formed complices with protein in the wort, precipitated, and were then filtered out together in the next stage, resulting in phenolic compounds being present in beer brewing byproducts.

4.3.1. Phenolic acids

Spent grains contains ferulic acid, *p*-coumaric acid, caffeic acid, syringic acid vanillic acid, and *p*-hydroxybenzoic acid. Among these, one study observed that the content of ferulic acid was the highest [10, 33].

4.3.2. Prenylflavonoids

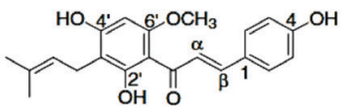
Prenylflavonoids are a subclass of flavonoids with a prenyl group of aromatic rings. Based on whether they have an open ring structure, they are divided into prenylchalcones and prenylflavanones (**Figure 2**) [34]. If prenylchalcones have a methoxy group attached to C6 in the aromatic ring, they are xanthohumol, whereas if they have a hydroxyl group attached, they are desmethylxanthohumol. If prenylflavanones have a methoxy group attached to C5 in the aromatic ring, they are isoxanthohumol, whereas if they have a hydroxyl attached, they are 8-prenylnaringenin.

To date, related studies on prenylflavonoids have mainly focused on prenylflavonoids in relation to beer and hops. Most prenylchalcones in hops and beer were xanthohumol and dexmethylxanthohumol, whereas most prenylflavanones were isoxanthohumol, 6-prenylnaringenin, and 8-prenylnaringenin [35].

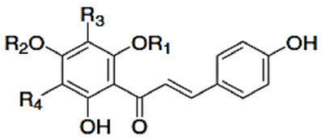
Regarding byproducts, Kao and Wu [36] indicated that beer lees contained isoxanthohumol (36.22 μg/g), xanthohumol (7.84 μg/g), 8-prenylnaringenin (19.17 μg/g), and 6-prenylnaringenin (29.56 μg/g). Lin [29] reported that surplus yeasts were most abundant in isoxanthohumol, followed by xanthohumol, 6-prenylnaringenin, and 8-prenylnaringenin. Spent hops contained mainly xanthohumol, followed by isoxanthohumol and 6-prenylnaringenin.

http://dx.doi.org/10.5772/intechopen.76126

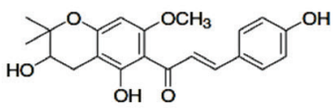
Chalcones



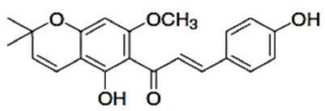
Xanthohumol



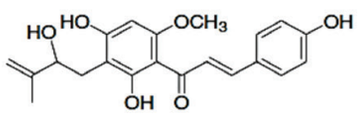
R1-R3 = H; R4 = Prenyl	Desmethylxanthohumol
R1, R3 = H; R2 = Me; R4 = Prenyl	Xanthogalenol
R1, R2 = Me; R3 = H; R4 = Prenyl	4'-*O*-Methylxanthohumol
R1-R3 = H, R4 = Geranyl	3'-*O*-Geranylchalconaringenin
R1, R2 = H; R3, R4 = Prenyl	3',5'-*O*-Diprenylchalconaringenin
R1 = Me; R2 = H; R3, R4 = Prenyl	5'-Prenylxanthohumol
R1, R2 = Me; -R3, R4 = H	Flavokawin



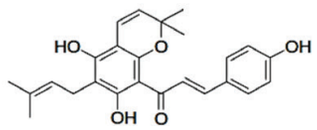
Xanthohumol B



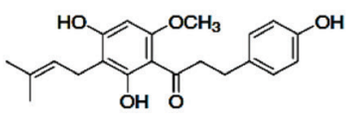
Xanthohumol C



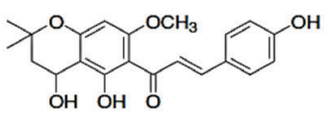
Xanthohumol D



Xanthohumol E

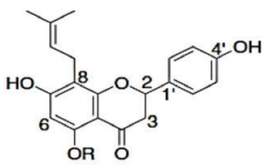


α,β-Dihydroxanthohumol

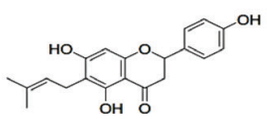


iso-Dehydrocycloxanthohumol hydrate

Flavanones



R = H, 8-Prenylnaringenin
R = Me, Isoxanthohumol



6-Prenylnaringenin

Figure 2. Prenylated chalcones and flavanones from hops Stevens and Page [34].

Surplus yeasts contained most types of prenylflavonoids but spent hops had higher prenylflavonoid content.

4.3.3. Hop bitter acids

The secondary metabolites of hops include hop bitter acids, volatile oil, and polyphenols. Hop bitter acids are divided into α-acids, or "humulone," and β-acids, or "lupulone," both of which are derivatives of prenylated phloroglucinol [37] (**Figure 3**). Based on the side chains on the acyl group, hop bitter acids can be divided into five types; those that start with "n," "co," "ad," "pre," and "post" are isovaleroyl-, isobutyroyl-, 2-methylbutyrol-, isohexanoyl-, and propanoyl-, respectively. The compositions and contents of α-acids and β-acids differ according to the type of hops and their growth conditions.

4.3.3.1. α-Acids

The dominant bitter acids in hops are α-acids, which are categorized as cohumulone, humulone, adhumulone, prehumulone, and posthumulone. Among these, the contents of cohumulone,

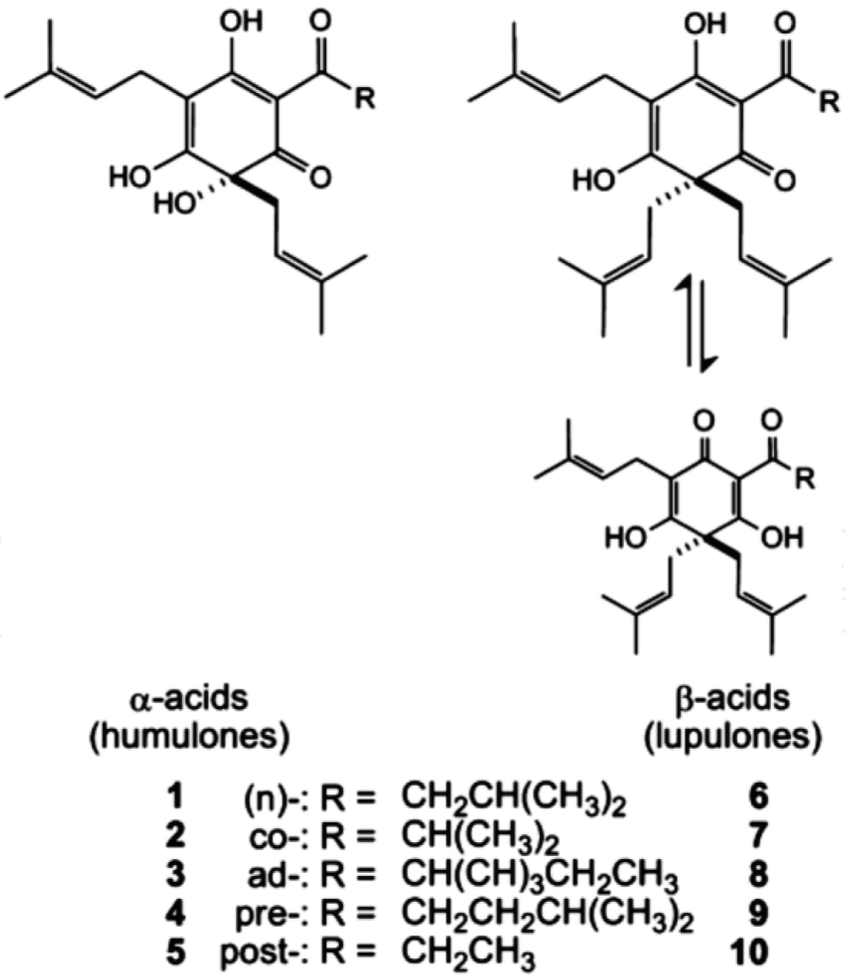


Figure 3. Structures of hop α-acids and β-acids Van Cleemput et al [37].

humulone, and adhumulone were higher, accounting for 35–70%, 20–65%, and 10–15% of α-acids, respectively [38]. Because α-acids are less water soluble and because during wort boiling, α-acids isomerize into iso-α-acids that are more water soluble, only approximately 25% of α-acids are retained in beer [6].

4.3.3.2. β-Acids

β-acids mainly exists in hops in the forms of lupulone and colupulone, both of which accounted for20–55% of the total β-acid content; adlupulone accounted for 10–15% and the contents of prelupulone and postlupulone were very low [37].

Because the tertiary alcohol on the C6 in β-acids is replaced by a prenyl side chain, its acidity is lower than that in α-acids. β-acids are highly sensitive to oxygen; they can easily autoxidize into stable hulupones, which include cohulupone, hulupone, and adhulupone [39]. Hulupones exist in matured hops and beer at degrees of condensation of 2–10 ppm, and provide beer with a bitter taste. Hulupones degrade into hulupinic acid, which is not bitter. The content of β-acids in beer is lower than that of α-acids, and thus β-acids do not considerably affect beer quality [40].

4.3.3.3. Iso-α-acids

During the wort boiling process, α-acids isomerize through the acyloin-type ring into iso-α-acids. The condensation of iso-α-acids in beer is a low 15–100 ppm; however, these acids are the source of 80% of the bitter taste in beer [41].

When heating α-acids in an alkaline solution containing divalent cations such as magnesium ion or calcium ion as a catalyst for isomerization, α-acids become *cis*-isomers and *trans*-isomers at a ratio of 1 to 1 [42]. When iso-α-acids are placed under ultraviolet and visible light (350–500 nm) with photosensitizers such as riboflavin, photo-oxidation occurs to break the side chain on C4, forming dehydrohumulinic acid and 3-methyl-2-butene-1-thiol, which is also known as "skunky thiol" because it is the main source of unfavorable flavors in beer. In addition, through reduction, iso-α-acids create *trans*-dihydro-isohumulones, and also *trans*-tetrahydro-isohumulones and *trans*-hexahydro-isohumulones, both of which can stabilize the foam produced by beer [37].

4.3.3.4. Hop bitter acids in brewing byproducts

Kao and Wu [36] discovered cohumulone, humulone, adhumulone, colupulone, lupulone], and adlupulone in beer lees. Among these components, humulone was the most dominant. Lin [29] reported findings of 8017 and 1130 μg/g of hop bitter acids in spent hops and surplus yeast, respectively. The hop bitter acids detected in spent hops were cohulupone, hulupone, adhulupone, *trans*-isocohumulone, *trans*-isohumulone, *trans*-isoadhumulone, cohumulone, humulone, adhumulone, prehumulone, adprehumulone, colupulone, lupulone, adlupulone, prelupulone, and adprelupulone. The same bitter acids were detected in surplus yeasts, except for *trans*-isocohumulone, prelupulone, and adprelupulone. In spent hops, colupulone had the highest content, with lupulone second. In surplus yeasts, humulone had the highest content, followed by colupulone.

5. Health benefits and potential of byproducts from beer brewing

To date, insufficient research has been devoted to the physiological functions of byproducts from beer brewing. However, these byproducts are rich in prenylflavonoids and hop bitter acids, which, as proven by many studies, have several health benefits that are detailed in this section. Therefore, beer brewing byproducts may have specific physiological activities. This section organizes physiological activities observed in previous studies, however, further research is required to clarify the physiological functions of the byproducts of beer brewing.

5.1. Antiobesity

Surplus yeast hinders the survival ratios of preadipocytes and adipocytes and can reduce cell apoptosis. The surplus yeast extract process arrests preadipocytes at G2/M, and cyclin B1 (a protein related to the cell cycle) substantially increases in number. Adding surplus yeast extract during the process of preadipocyte differentiation into adipocytes effectively reduces the number of adipocytes and hinders the formation of triglycerides [43].

Animal models have proven that feeding of brewer's yeast biomass with ethanol extract to male Sprague-Dawley rats could reduce the weight of fat around the kidneys and paraplegia, reduced triglyceride content in serum and the liver, and increased antioxidant capacity in the liver [44].

When xanthohumol and isoxanthohumol treated preadipocyte 3T3-L1, the expressions of transcription factors for lipid metabolism reduced, hence preventing fat tissue from forming and inducing apoptosis of adipocytes [45]. Xanthohumol could suppress the weight of rats with high-fat diets, reduce weight gain around the liver, and reduce the triglyceride content in their serum and liver [46].

5.2. Antiproliferation of cancer cells

Surplus yeasts extract in non-small cell lung carcinoma A549 increased the protein expression from those of the mitogen-activated protein kinase family, including p-ERK1/2, p-JNK, and p-p38, and suppressed the expression of cyclin E1 and arrested the cell cycle at G0/G1, thereby reducing the survival of A549 cells. In H460 lung cancer cells, surplus yeast extract significantly increased the expressions of proteins p-ERK1/2 and p-p38 and decreased the protein content of cyclin D1 and cyclin E1, thereby arresting cell cycle at G0/G1. The main suppressants in these two experiments were xanthohumol and hop bitter acids [47].

5.3. Anti-inflammatory activity

Studies have shown that xanthohumol, β-acids and hexahydro-β-acids could suppress the generation of chemokine and cytokine, as well as their gene expression in inflammatory cells [48, 49]. In animal models, xanthohumol was considered effective in reducing liver inflammation, thereby minimizing liver fibrosis [50].

Hop bitter acids could suppress the activation of nuclear factor-κB (NF-κB) in liver astrocytes, and could also suppress the generation of monocyte chemoattractant protein-1 (MCP-1) and α-smooth muscle actin (α-SMA) to achieve anti-inflammatory and antifibrotic outcomes [51]. In an animal test, feeding 1.25 g of hop extract to LPS-induced mice for 10 days reduced the PGE2 content in their blood [52].

5.4. Antioxidant activity

Feeding xanthohumol to rats with chemical hepatitis could increase the glutathione content and the activities of antioxidant enzymes in liver [53]. Dorn et al. [54] reported that after xanthohumol treatment, the active oxygen content due to ischemia–reperfusion injury had reduced. In addition, isoxanthohumol was able to remove active oxygen [55].

Iso-α-acids, α-acids, and β-acids all have the abilities to clear the peroxynitrite free radical and reduce lipid peroxidation [56]. Namikoshi et al. [57] reported that the rat kidneys on a high-salt diet produced excessive amounts of active oxygen, resulting in kidney tissue damage due to oxidation. Iso-α-acids were able to suppress the formation of active oxygen to achieve the goal of antioxidation.

5.5. Estrogen activity

8-prenylnaringenin exhibited a structure similar to that of estrogen and could be bound with estrogen acceptors, indicating that 8-prenylnaringenin also exhibited activity similar to that of estrogen [58]. Christoffel et al. [59] reflected that feeding Sprague Dawley rats 8-prenylnaringenin for 3 months could reduce the content of follicle-stimulating hormone and luteinizing hormone in serum, increase the weight of the uterus, and stimulate the secretion of insulin-like growth factor I and prolactin.

5.6. Antiangiogenesis

Xanthohumol could suppress the formation of vascular endothelial growth factor (VEGF) and interleukin-8 in pancreatic cancer cells, and the antiangiogenesis effect was achieved through suppressing NF-κB [60].

Shimamura et al. [61] proved that 100 μM of humulone was effective in suppressing the formation of the VEGF and could prevent angiogenesis from Co26s cells. An amount of 2.5 to 50 μg/mL of lupulone could suppress the proliferation of human umbilical vein endothelial cells and the secretion of fibronectin.

5.7. Anticancer activity

Xanthohumol, isoxanthohumol, 8-prenylnaringenin, and 6-prenylnaringnin were all effective in suppressing the proliferation of human prostate cancer cells PC-3 and DU145 [62]. In addition, xanthohumol was able to reduce gene expressions related to the NOTCH1 pathway, thereby arresting the cell cycle of human ovarian carcinoma cells SKOV3 and OVCAR3 in the G2/M period and further causing apoptosis [63].

Festa et al. [64] revealed that xanthohumol activated caspase-3 and caspase-9, through mitochondrial depolarization, releasing cytochrome C, reducing Bcl-2 protein expression, and increasing the oxidation pressure, causing apoptosis of human glioblastoma multiforme tumor cell (T98G). Xanthohumol could prevent carcinogen metabolites from being processed by phase I enzymes (e.g. cytochrome P450) or activated by cytochrome isomers (e.g., cytochrome 1A1 and cytochrome 1A2). Xanthohumol was also able to promote carcinogens excreted from human body by increase their water-solubility that effected by phase II enzymes (glutathione S-transferase and UDP-glucuronyl transferase) [34].

Apoptosis of HL-60 (human promyelocytic leukemia cells) and SW 620 (human colorectal adenocarcinoma cells) can be induced by β-acids and α-acids [65]. Yasukawa et al. [66] maintained that humulone can suppress tumor formation in mice treated by 7,12-dimethylbenz[a] anthracene.

5.8. Antianxiety activity

In contrast to β-acids, which are sedatives, α-acids are the major anxiolytic substances in hops [67]. Therefore, through *r*-aminobutyric acid A receptors, 5-hydroxytryptamine receptors, and melatonin, hops were able to alter the central nervous system to achieve the effects of sedation and sleep quality improvement [68].

5.9. Metabolic syndrome prevention

Isohumulones could activate peroxisome proliferator activated receptors α (PPARα) to increase sensitivity to insulin and help protect against type II diabetes [69]. Miura et al. [70] revealed that isohumulone could increase the mRNA expressions of acyl-CoA oxidase, acyl-CoA synthetase, the fatty acid transport protein, and lipoprotein lipase and reduce the mRNA activity of Apo CIII to achieve regulation of liver lipid synthesis.

5.10. Antiosteoporosis

Tobe et al. [71] discovered that α-acids were able to suppress dentin bone loss but that cohumulone was unable to exert the suppression effect. The researchers also discovered that β-acids were the most effective acids in suppressing dentin bone loss. Ding et al. [72] have evaluated cytokines such as interleukin-6 and TNF-α in serum and have proven that the cytokine content had a negative correlation with bone mass. Therefore, the effect of hop bitter acids on inflammation could be applied for osteoporosis prevention and treatments.

6. Conclusion

Prenylflavonoids and hop bitter acids are the most important functional components from hop, and they may remain in the byproducts especially spent hops and surplus yeasts during beer brewing. Both prenylflavonoids and hop bitter acids have been confirmed to possess

many physiological activities in current research, but studies for establishing the proper health benefit of beer brewing byproducts remained uncertain. As mentioned in the preceding section, the future considerations and latent problems have to be emphasized. First, beer brewing technology should be optimized in order to minimize the amounts of waste arising. Second, methods for complete recovery of by-products during beer brewing on a large scale and at an affordable level should be developed. Third, specific analytical methods for the characterization and quantification of organic micronutrients and other functional compounds need to be built. Fourth, the bioactivity, bioavailability and toxicology of the functional components in beer brewing byproducts need to be carefully assessed by *in vitro* and *in vivo* studies.

Acknowledgements

This review was supported by a grant (104-2221-E-030-018-MY2, 106-2221-E-030-015) from Taiwan National Science Council, and Office Research and Development from Fu Jen University.

Author details

Tsai-Hua Kao

Address all correspondence to: 072500@mail.fju.edu.tw

Department of Food Science, Fu Jen Catholic University, Taipei, Taiwan

References

[1] Kumar SR. In: Chandrasekaran M, editor. Valorization of Food Processing By-products. Boca Raton, Florida, USA: CRC Press; 2012

[2] Mussatto SI. Biotechnological potential of brewing industry by-products. In: Singh nee' Nigam P, Pandey A, editors. Biotechnology for Agro-industrial Residues Utilization. Berlin, Germany: Springer; 2009. pp. 313-326

[3] Protz R. The ultimate encyclopedia of beer: The definitive guide to the world's great brews. New York: Smithmark Publishing; 1995

[4] Mussatto SI, Dragone G, Roberto IC. Brewer's spent grain: Generation, characteristics and potential applications. Journal of Cereal Science. 1995;**43**:1-14. DOI: 10.1016/j.jcs.2005.06.001

[5] Briggs DE, Boulton CA, Brookes PA, Stevens R. Brewing: Science and Practice. Cambridge: Woodhead Publishing; 2004

[6] De Keukeleire DD. Fundamentals of beer and hop chemistry. Quimica Nova. 2000;**23**: 108-112

[7] Hartmeier W, Reiss M. Production of beer and wine. In: Industrial Applications. 2nd ed. Berlin, Germany: Springer; 2010. pp. 59-77

[8] Mussatto SI, Roberto IC. Chemical characterization and liberation of pentose sugars from brewer's spent grain. Journal of Chemical Technology & Biotechnology. 2006;**81**:268-274. DOI: 10.1002/jctb.1374

[9] Adelagun ROA, Itodo AU, Berezi EP, Oko OJ, Kamba EA, Andrew C, Bello HA Adsorptive removal of Cd^{2+} and Zn^{2+} from aqueous system by BSG. Journal of Chemistry and Materials Research. 2014;**6**:104-112

[10] Mussatto SI, Dragone G, Roberto IC. Feruic and *p*-coumaric acids extraction by alkaline hydrolysis of brewer's spent grain. Industrial Crops & Products. 2007;**25**:231-237. DOI: 10.1016/j.indcrop.2006.11.001

[11] Aliyu S, Bala M. Brewer's spent grain: A review of its potentials and applications. African Journal of Biotechnology. 2011;**10**:324-331. DOI:10.5897/AJBx10.006

[12] Stojceska V, Ainsworth P, Plunkett A. The recycling of brewer's processing by-product into ready-to-eat snacks using extrusion technology. Journal of Cereal Science. 2008;**47**:469-479. DOI: 10.1016/j.jcs.2007.05.016

[13] Silva JP, Sousa S, Rodrigues J, Antunes H, Porter JJ, Goncalves I, Ferreira-Dias S. Adsorption of acid orange 7 dye in aqueous solutions by spent brewery grains. Separation and Purification Technology. 2004;**40**:309-315. DOI: 10.1016/j.seppur.2004.03.010

[14] Mussatto SI, Fernandes M, Dragone G. Brewer's spent grain as raw material for lactic acid production by *Lactobacillus delbrueckii*. Biotechnology Letters. 2007;**29**:1973-1976. DOI: 10.1007/s10529-007-9494-3

[15] Xiros C, Christakopouls P. Biotechnological potential of brewers spent grain and its recent applications. Waste and Biomass Valorization. 2012;**3**:213-332. DOI: 10.1007/s12649-012-9108-8

[16] Benitez JL, Forster A, De Keukeleire D, Moir M, Sharpe FR, Verhagen LC, Westwood KT. Hops and Hop Products. Nurnberg, Germany: Verlag Hans Carl; 1997

[17] Oosterveld A, Voragen AGJ, Schols HA. Characterization of hop pectins shows the presence of an arabinogalactan-protein. Carbohydrate Polymers. 2002;**49**:407-413. DOI: 10.1016/S0144-8617(01)00350-2

[18] Wallen SE, Marshall Jr HF. Protein quality evaluation of spent hops. Journal of Agricultural and Food Chemistry. 1979;**27**:635-636. DOI: 10.1021/jf60223a027

[19] Huszcza E, Bartmańska A. The implication of yeast in debittering of spent hops. Enzyme and Microbial Technology. 2008;**42**:421-425. DOI: 10.1016/j.enzmictec.2008.01.004

[20] Laufenberg G, Kunz B, Nystroem M. Transformation of vegetable waste into value added products: (A) the upgrading concept; (B) practical implementation. Bioresource Technology. 2003;**87**:167-198

[21] Fischer K, Bipp HP. Generation of organic acids and monosaccharides by hydrolyti-cand oxidative transformation of food processing residues. Bioresource Technology. 2005;**96**:831-842. DOI: 10.1016/j.biortech.2004.07.003

[22] Soares EV, Soares HM. Cleanup of industrial effluents containing heavy metals: a new opportunity of valorising the biomass produced by brewing industry. Applied Microbiology and Biotechnology. 2013;**97**:6667-6675. DOI: 10.1007/s00253-013-5063-y

[23] Chae HJ, Joo H, In MJ. Utilization of brewer's yeast cells for the production of food-grade yeast extract. Part I: Effects of different enzymatic treatments on solid and protein recovery and flavor characteristics. Bioresource Technology. 2001;**76**:253-258. DOI: 10.1016/S0960-8524(00)00102-4

[24] Rakin M, Vukasinovic M, Siler-Marinkovic S. Contribution of lactic acid fermentation to improved nutritive quality vegetable juices enriched with brewer's yeast autolysate. Food Chemistry. 2007;**100**:599-602. DOI: 10.1016/j.foodchem.2005.09.077

[25] Thammakiti S, Suphantharika M, Phaesuwan T. Preparation of spent brewer's yeast-glucans for potential applications in the food industry. International Journal of Food Science & Technology. 2004;**39**:21-29. DOI: 10.1111/j.1365-2621.2004.00742.x

[26] Parvathi K, Nagendran R, Nareshkumar R. Lead biosorption onto waste beer yeast by-product, a means to decontaminate effluent generated from battery manufacturing industry. Electronic Journal of Biotechnology. 2007;**10**:92-105. DOI: 10.2225/vol10-issue1-fulltext-13

[27] Russ W, Mörtel H, Meyer-Pittroff R. Application of spent grains to increase porosity in bricks. Construction and Building Materials. 2005;**19**:117-126. DOI: 10.1016/j.conbuildmat.2004.05.014

[28] Gromes R, Zeuch M, Piendl A. Further investigations into the dietary fibre content of beers. Brau International. 2000;**18**:24-28

[29] Lin TI. Content and variety of functional components in hops, beer and brewer's by-products [thesis]. Taipei: Fu Jen University; 2016

[30] Lewis MJ, Young TW. Brewing. London, UK: Chapman and Hall; 1995

[31] Bamforth CW. Nutritional aspects of beer-a review. Nutrition Research. 2002;**22**:227-237. DOI: 10.1016/S0271-5317(01)00360-8

[32] Gorjanovic S, Novakovic M, Potkonjak N, Leskosek-Cukalovic I, Suznjevic D. Application of a novel antioxidative assay in beer analysis and brewing process monitoring. Journal of Agricultural and Food Chemistry. 2010;**58**:744-751. DOI: 10.1021/jf903091n

[33] Bartolome B, Faulds CB, Williamso G. Enzymic release of ferulic acid from barley spent grain. Journal of Cereal Science. 1997;**25**:285-288. DOI: 10.1006/jcrs.1996.0091

[34] Stevens JF, Page JE. Xanthohumol and related prenylflavonoids from hops and beer: to your good health! Phytochemistry. 2004;**64**:1317-1330. DOI: 10.1016/j.phytochem.2004.04.025

[35] Stevens JF, Taylor AW, Deinzer ML. Quanitative analysis of xanthohumol and related prenylflavonoids in hops and beer : by liquid chromatography-tandem mass spectrometry. Journal of Chromatography A. 1999;**832**:97-107. DOI: 10.1016/S0021-9673(98)01001-2

[36] Kao TH, Wu GY. Simultaneous determination of prenylflavonoid and hop bitter acid in beer lee by HPLC-DAD-MS. Food Chemistry. 2013;**141**:1218-1226. DOI: 10.1016/j.foodchem.2013.04.032

[37] Van Cleemput M, Cattoor K, Bosscher KD, Haegeman G, Keukeleire DD, Heyerick A. Hop (*Humulus lupulus*)-derived bitter acids as multipotent bioactive compounds. Journal of Natural Products. 2009;**72**:1220-1230. DOI: 10.1021/np800740m

[38] Shah BN, Panchal MA, Gohil N, Nayak BS, Modi DC. Phyto-pharmacol profile of *Humulus lupulus*. Pharmacology. 2010;**1**:719-736

[39] Haseleu G, Intelmann D, Hofmann T. Identification and RP-HPLC-ESI-MS/MS quantitation of bitter-tasting β-acid transformation products in beer. Journal of Agricultural and Food Chemistry. 2009;**57**:7480-7489. DOI: 10.1021/jf901759y

[40] Verzele M. 100 years of hop chemistry and its relevance to brewing. Journal of the Institute of Brewing.1986;**92**:32-48. DOI: 10.1002/j.2050-0416.1986.tb04372.x

[41] Blanco CA, Rojas A, Caballero PA, Ronda F, Gomez M, Caballero I. A better control of beer properties by predicting acidity of hop iso-α-acids. Trends in Food Science and Technology. 2006;**17**:373-377. DOI: 10.1016/j.tifs.2005.11.012

[42] Moir M. Hops: a millennium review. Journal of the American Society of Brewing Chemists. 2000;**58**:131-146. DOI: 10.1094/ASBCJ-58-0131

[43] Wu GY. Analysis of functional components in beer lee and its antiobesity activities [thesis]. Taipei: Fu Jen University; 2012

[44] Chuang ZL. Anti-obesity effect of brewer's yeast biomass in animal model [thesis]. Taipei: Fu Jen University; 2013

[45] Kiyofuji A, Yui K, Takahashi K, Osada K. Effects of xanthohumol-rich hop extract on the differentiation of preadipocytes. Journal of Oleo Science. 2014;**63**:593-597. DOI: 10.5650/jos.ess14009

[46] Yui K, Kiyofuji A, OK. Effects of xanthohumol-rich extract from the hop on fatty acid metabolism in rats fed a high-fat diet. Journal of Oleo Science. 2014;**63**:159-168. DOI: 10.5650/jos.ess13136

[47] Lin CY. Antiproliferative effect of ethanol extract from beer brewer's yeast biomass in lung cancer cell lines [thesis]. Taipei: Fu Jen University; 2013

[48] Lee IS, Lim J, Gal J, Kang JC, Kim HJ, Kang BY, Choi HJ. Anti-inflammatory activity of xanthohumol involves heme oxygenase-1 induction via NRF2-ARE signaling in microglial BV2 cells. Neurochemistry International. 2011;**58**:153-160. DOI: 10.1016/j.neuint.2010.11.008

[49] Tang W, Chen LH, Daun H, Ho CT, Pan MH. Inhibitory effects of hexahydro-β-acids in LPS-stimulated murine macrophage. Journal of Functional Foods. 2011;**3**:215-222. DOI: 10.1016/j.jff.2011.04.004

[50] Dorn C, Massinger S, Wuzik A, Heilmann J, Hellerbrand C. Xanthohumol suppresses inflammatory response to warm ischemia-reperfusion induced liver injury. Experimental and Molecular Pathology. 2013;**94**:10-16. DOI: 10.1016/j.yexmp.2012.05.003

[51] Saugspier M, Dorn C, Thasler WE, Heilmann J, Hellerbrand C. Hop bitter acids exhibit anti-fibrogenic effects on hepatic stellate cells *in vitro*. Experimental and Molecular Pathology. 2011;**92**:222-228. DOI: 10.1016/j.yexmp.2011.11.005

[52] Hougee S, Faber J, Sanders A, van den Berg WB, Garssen J, Smit HF, Hoijer MA: Selective inhibition of COX-2 by a standardized CO2 extract of *Humulus lupulus* L. in *vitro* and its activity in a mouse model of zymosan-induced arthritis. Planta Medica. 2006;**72**:228-233

[53] Pinto C, Duque AL, Rodríquez-Galdón B, Cestero JJ, Macías P. Xanthohumol prevents carbon tetrachloride-induced acute liver injury in rats. Food and Chemical Toxicology. 2012;**50**:3405-3412. DOI: 10.1016/j.fct.2012.07.035

[54] Dorn C, Heilmann J, Hellerbrand C. Protective effect of xanthohumol on toxin-induced liver inflammation and fibrosis. International Journal of Clinical and Experimental Pathology. 2012;**5**:29-36

[55] Gerhauser C, Alt A, Heiss E, Gamal-Eldeen A, Klimo K, Knauft J, Neumann I, Scherf H-R, Frank N, Bartsch H, Becker H. Cancer chemopreventive activity of xanthohumol, a natural product derived from hop. Molecular Cancer Therapeutics. 2002;**1**:959-969

[56] Liu Y, Gu X, Tang J, Liu K. Antioxidant activities of hops (*Humulus lupulus*) and their products. Journal of the American Society of Brewing Chemists. 2007;**65**:116-121. DOI: 10.1094/ASBCJ-2007-0211-01

[57] Namikoshi T, Tomita N, Fujimoto S, Haruna Y, Ohzeki M, Komai N, Sasaki T, Yoshida A, Kashihara N. Isohumulones derived from hops ameliorate renal injury via an anti-oxidative effect in Dahl salt-sensitive rats. Hypertension Research. 2007;**30**:175-184. DOI: 10.1291/hypres.30.175

[58] Milligan S, Kalita J, Pocock V, Heyerick A, De Cooman L, Rong H, De KD. Oestrogenic activity of the hop phyto-oestrogen, 8-prenylnaringenin. Reproduction. 2002;**123**:235-242. DOI: 10.1530/rep.0.1230235

[59] Christoffel J, Rimoldi G, Wuttke W. Effects of 8-prenylnaringenin on the hypothal-amo-pituitary-uterine axis in rats after 3-month treatment. Journal of Endocrinology. 2006;**188**:397-405. DOI: 10.1677/joe.1.06384

[60] Shamoto T, Matsuo Y, Shibata T, Tsuboi K, Takahashi H, Funahashi H, Okada Y, Takeyama H. Xanthohumol inhibits angiogenesis through VEGF and IL-8 in pancreatic cancer. Pancreatology. 2013;**13**:S52-S53. DOI: 10.1016/j.pan.2013.07.203

[61] Shimamura M, Hazato T, Ashino H, Yamamoto Y, Iwasaki E, Tobe H, Yamamoto K, Yamamoto S. Inhibition of angiogenesis by humulone, a bitter acid from beer hop. Biochemical and Biophysical Research Communications. 2001;**289**:220-224. DOI: 10.1006/bbrc.2001.5934

[62] Zanoli P, Zavatti M. Pharmacognostic and pharmacological profile of *Humulus lupulus* L. Journal of Ethnopharmacology. 2008;**116**:383-396. DOI: 10.1016/j.jep.2008.01.011

[63] Drenzek JG, Seiler NL, Jaskula-Sztul R, Rausch MM, Rose SL. Xanthohumol decreases Notch1 expression and cell growth by cell cycle arrest and induction of apoptosis in epithelial ovarian cancer cell lines. Gynecologic Oncology. 2011;**122**:396-401. DOI: 10.1016/j.ygyno.2011.04.027

[64] Festa M, Capsso A, D'Acunto CW, Masullo M, Rossi AG, Pizza C, Piacente S. Xanthohumol induces apoptosis in human malignant glioblastoma cells by increasing reactive oxygen species and activating MAPK pathways. Journal of Natural Products. 2011;**74**:2505-2513. DOI: 10.1021/np200390x

[65] Lamy V, Roussi S, Chaabi M, Gossé F, Schall N, Lobstein A, Raul F. Chemopreventive effects of lupulone, a hop β-acid, on human colon cancer-derived metastatic SW620 cells and in a rat model of colon carcinogenesis. Carcinogenesis. 2007;**28**:1575-1581. DOI: 10.1093/carcin/bgm080

[66] Yasukawa K, Takeuchi M, Takido M. Humulone, a bitter in the hop, inhibits tumor promotion by 12-0-tetradecanoylphorbol-13-acetate in two-stage carcinogenesis in mouse skin. Oncology. 1995;**52**:156-158. DOI: 10.1159/000227448

[67] Zanoli P, Zavatti M, Rivasi M, Brusiani F, Losi G, Puia G, Avallone R, Baraldi M. Evidence that the β-acids fraction of hops reduces central GABAergic neurotransmission. Journal of Ethnopharmacology. 2007;**109**:87-92. DOI: 10.1016/j.jep.2006.07.008

[68] Sanchez CL, Franco L, Bravo R, Rubio C, Rodríguez AB. Beer and health: benefits for sleep. Revista Española de Nutrición Comunitaria. 2010;**16**:160-163

[69] Yajima H, Ikeshima E, Shiraki M, Kanaya T, Fujiwara D, Odai H, Tsuboyama-Kasaoka N, Ezaki O, Oikawa S, Kondo K. Isohumulones, bitter acids derived from hops, activate both peroxisome proliferator-activated receptor α and γ and reduce insulin resistance. Journal of Biological Chemistry. 2004;**279**:33456-33462. DOI: 10.1074/jbc.M403456200

[70] Miura Y, Hosono M, Oyamada C, Odai H, Oikawa S, Kondo K. Dietary isohumulones, the bitter components of beer, raise plasma HDL-cholesterol levels and reduce liver cholesterol and triacylglycerol contents similar to PPARα activations in C57BL/6 mice. British Journal of Nutrition. 2005;**93**:559-567. DOI: 10.1079/BJN20041384

[71] Tobe H, Muraki Y, Kitamura K, Komiyama O, Sato Y, Sugioka T, Maruyama HB. Bone resorption inhibitors from hop extract. Bioscience, Biotechnology, and Biochemistry. 1997;**61**:158-159. DOI: 10.1271/bbb.61.158

[72] Ding C, Parameswaran V, Udayan R, Burgess J, Jones GJ. Circulating levels of inflammatory markers predict change in bone mineral density and resorption in older adults: A longitudinal study. The Journal of Clinical Endocrinology and Metabolism. 2008;**93**:1952-1958. DOI: 10.1210/jc.2007-2325