"Beer - bitter and healthy"

POSSIBILITIES FOR USE IN MEDICINE | The xanthohumol hop component in particular has been a focus of interest for some time. It has an extraordinarily wide spectrum of pharmacologically positive action, above all highly promising cancer chemo-preventive potential. The compound 8-prenylnaringenine found in hops in traces only is also becoming increasingly important due to its estrogenic properties.

THE HOPE OF FINDING alternative possibilities for use of hops in medicine is based on the active potential of these two substances. This could indirectly reflect positively on beer as a healthy beverage, it being hitherto the only food containing this raw material.

In parallel, the pharmacological profile of the iso-alpha acids and isoxanthohumol beer components has also been investigated in more detail in recent years. It is known that both compounds originate from hops and are formed by isomerisation reactions during wort boiling (Fig. 1). These investigations also show up diverse positive characteristics. All hitherto published relevant studies come from Japan. Kondo was the first to report on these studies at the 2003 EBC Congress [1]. Several scientific publications on this topic have meantime been reproduced in international specialised journals. First patent applications have been filed. This contribution summarises and discusses the relevant results.

Ilsoxanthohumol and osteoporosis

Although the isomerised form has hitherto been classified as overall less active than xanthohumol, in particular a patent application from Japan has brought it to the fore [2]. It involves a multiplicity of products (tablets, food, beverages) which prevent or mitigate or even reverse a decrease in bone mineral density. Brittle bones are mainly caused by osteoporosis which may arise in women after menopause when production of endogenous oestrogen decreases. Isoxanthohumol has been identified as active com-

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ponent ("First claim: A composition for the inhibition or prevention of a bone mineral density reduction, comprising isoxanthohumol as an active ingredient"). Relatively low dosages without estrogenic side effects are already classified as effective (following on from animal tests). The patent application covers food specially enriched with isoxanthohumol such as tea, milk or yoghurt. Conventional beer cannot be patented because its isoxanthohumol content has been known long before the application was filed ("In general, hop-derived food and drink such as beer, alcohol-free beer, and low-malt beer sometimes already contain a given or larger amount of the active ingredient according to the present invention").

It is an assured epidemiological fact that moderate consumption of alcoholic beverages can increase bone mineral density. This effect is generally attributed to intake of alcohol and, in the case of beer, also especially to its relatively high silicon content (10 - 40 mg per litre), as has recently been reported at the 4th Beer & Health Symposium in Brussels [3] (lecture by Powell, J.: "Beer, silicon and bones"). The properties of isoxanthohumol described in the patent application are a further argument in favour of the preventive effect of beer.

Ilsoxanthohumol in beer

As presented at the 2005 EBC Congress, isoxanthohumol is classified as a bitter substance [4]. The taste threshold has been determined at 0.5 mg per litre in an unhopped Pilsner beer, a value exceeded in many beers. Compared to standard hopping, tasting tests of isoxanthohumol led to a positive assessment of bitterness (intensity: less, qual-

ity: balanced, less lingering). Depending on hopping (dosed quantity, hop product used) and the brewing process employed, conventional beers can contain up to about 3 mg of isoxanthohumol per litre [5]. Successful tests aimed at increasing this value further have already been carried out [6].

Iso-alpha acids and metabolic syndrome

In medicine, diseases relating to metabolic disorders are referred to as "metabolic syndrome". This refers to impairment of organ and cell functions (kidney, liver, fat cells and muscle cells) that result in symptoms such as high blood pressure, increased uric acid, blood fat and blood sugar values. Symptoms are inhibited blood circulation, blocking of blood vessels (arteries) and thus, ultimately, a myocardial infarction or a stroke (Fig. 2). Very different metabolic disorders of the metabolic syndrome interact and can influence and reinforce each other. A series of recently published studies shows that iso-alpha acids are among the natural substances that can mitigate such progress of the disease. Several publications report on a positive influence on lipometabolism. Only the most recent publication [7] will be mentioned here, this cites previous investigations in this area. It was found that, after

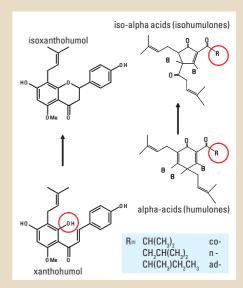


Fig. 1 Isomerisation processes during wort boiling

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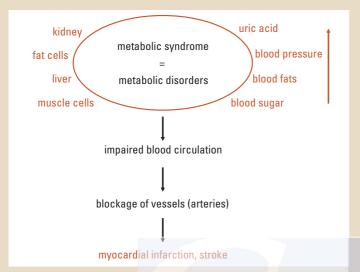


Fig. 2 Symptoms of metabolic syndrome

administration of fatty food to laboratory mice with and without addition of iso-alpha acids, the isomerised hop components significantly reduced weight gain and significantly increased fecal excretion of lipids. This would lead to the conclusion that iso-alpha acids could prevent obesity by inhibiting intestinal fat absorption. ("The inhibition of intenstinal dietary fat absorption may be the mechanism by which iso-alpha-acids induce its weight-lowering effects in high-fat diet-fed mice... These results suggest that iso-alpha-acids may be helpful in humans in preventing diet-induced obesity and perhaps even metabolic syndrome, the latter of which is known to be associated with obesity").

Investigations into the action of iso-alpha acids to counteract diabetes type 2 (adultonset diabetes) are furthest advanced. This disease is characterised by increased glucose levels in the blood (blood sugar) as a result of reduced effectiveness of endogenous insulin (insulin resistance). In vitro experiments and subsequent animal tests have

initially shown a very promising potential for prevention of disease symptoms.

The effect has meantime even been confirmed in a placebo-controlled clinical pilot study [8]. Twenty men and women (45 to type 2 were divided into two groups. One group received a placebo, the other group iso-alpha acids (2 x 80 mg/day). In contrast to the control group, significant decreases of blood sugar level and of blood pressure were noted within 8 weeks in the group taking iso-alpha acids daily. The physiological effectiveness in humans is thus proven ("Results of a preliminary clinical study indicated that isohumulones improved insulin sensitivity in type 2 diabetic patients Thus, isohumulones in beer are worth investigating further as therapeutic agents for the treatment of metabolic syndrome associated with insulin resistance").

Ilso-alpha acids in beer

Hence, iso-alpha acids show a promising potential for preventing or mitigating the

metabolic syndrome. Numerous results from animal tests are known and a first confirmation in humans is also available. In all investigations described in this article, the homologous mixtures (co-, nand ad-isohumolone) as are present in isomerised hop extracts and are also contained in every beer have been tested (Fig. 1). Depending on bitterness, the considerable amount, 5 mg to 40 mg of iso-alpha acids per litre, is found in beer. Such high concentrations of active compounds provide a very convincing argument in the discussion of positive health effects of moderate beer consumption. It is also known from epidemiological investigations that (regular) moderate intake of alcoholic beverages is protective against diabetes type 2 and weight gain. Beer is meantime classified as being as effective as red wine. Most recent investigations on this topic have also been presented at the 4th Beer & Health Symposium in Brus-65 years old) suffering from mild diabetes sels (Hendricks: "Diabetes type II, insuline sensitivity and beer"; Astrup: "Metabolic Syndrome and body weight: Where beer fits in"). A contribution of iso-alpha acids to the positive effect of beer is obvious, especially in this area.

> However, it should be noted that a clear trend towards less bitter beers can be seen for many years. Fig. 3 shows average alpha additions in breweries, these have dropped by almost 30% in the last 10 years. In-house investigations of international major beer brands (output >1 million hl per year) have shown that this is a worldwide trend.

> Bitterness and thus the iso-alpha acid levels in beer are going down in all parts of the world (Fig. 4). But it should be emphasised that relatively strongly hopped beers still play a market-dominating role in Germany.

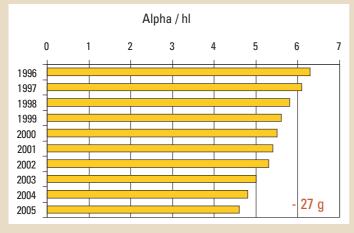


Fig. 3 Average dosage of alpha acids in breweries (worldwide)

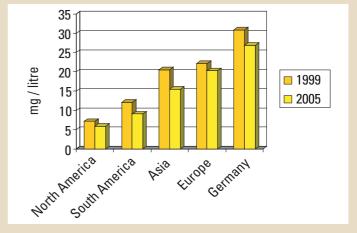


Fig. 4 Iso-alpha acids in major beer brands

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■Carcinostatic activity

Reports on carcinostatic properties of beer in animal tests repeatedly make the headlines. A recent publication, for example, describes the effect of freeze-dried beer in carcinogenesis of intestinal cancer in rats [9]. Strongly hopped beer was more active than unhopped beer, and iso-alpha acids could again be identified as the active components ("These observations suggest that isohumulones show chemopreventive effects").

Bohr [10] reports in his recent doctoral thesis that first investigations at the German Cancer Research Centre in Heidelberg also confirm the carcinostatic potential of iso-alpha acids. Especially the main bitter substances seem to also play a role in the potential of beer to protect against cancer. An adjunctive contribution of isoxanthohumol would be conceivable, its antimutagenic activity has been known for some time [11].

■Conclusion

Most recent results of pharmacological research show promising properties of the main bitter substances of beer, the iso-alpha acids, as well as of isoxanthohumol, also a beer bitter component. Numerous protective properties against a number of today's lifestyle-induced civilisation diseases could be ascertained (osteoporosis, metabolic syndrome, cancer).

Relevant investigations have already shown considerable progress. The resulting findings constitute convincing arguments in showing the positive effects of moderate beer consumption on health.

The discussion is increasingly revolving around hops as a raw material. In order to delineate beers from other alcoholic beverages (red wine), one should above all favour more strongly hopped beers - in accordance with the motto: "Beer - bitter and healthy".

References

- 1. Kondo, K., Proceedings of the 29th EBC Congress, 2003, p. 133.
- 2. Europäische Patentanmeldung EP 1 618875A1.
- 3. See: www.brewersofeurope.org.
- 4. Fritsch, H. et al., Proceedings of the 30th EBC Congress, 2005, p. 106.
- 5. Piendl, A., Biendl, M., Brauwelt International 18, 2000, p. 310.
- 6. Biendl, M. et al., Brauwelt International 22, 2004, p. 182.
- 7. Yajima, H. et al., Int. J. Obes. 29, 2005, p. 991.
- 8. Yajima, H. et al., J. Biol. Chem. 279, 2004, 33456.
- 9. Nozawa, H. et al., Mol. Nutr. Food Res. 49, 2005, p. 772.
- 10. Bohr, G., Diss<mark>ertation Universität des</mark> Saarlandes, 2005.
- 11. Miranda et al., Drug Met. Disp. 28, 2000, p. 1297.

Letter to Brauwelt International

My esteemed friends

Today I write to you to communicate a happy massage.

As end of January 2007, I will be leaving my active duties in the Efes Beer Group which I have carried on for thirty-four years. My departure is due to the retirement policy of our group. From now on, I will continue to contribute to our group as a member of the board of directors of some of the Anadolu Group companies, of which the Efes Beer Group is an affiliate.

In a couple of days, I will end my role in the Efes Beer Group as the group president, which started as a marketing specialist in 1973. Working for an uninterrupted period of thirtyfour years in our group, which has a history of thirty-eight years, and ending my career at the very top of the group is a source of happiness both for me and my family. Spending twenty-seven years of this thirtyfour years tenure at the general

manager position or above, in other words, being among the ones to direct the group's policies for twenty-seven years is also very honouring for me.

Efes Beer Group entered the Turkish beer market in the summer of 1969, with two breweries established in Istanbul and Izmir producing the "Efes Pilsen" brand, with a total brewing capacity of 30 million litres. Over the past thirty-eight years, our group did not only grow to become the number one in Turkey but also, through the international expansion strategies that were formulated in the 1980's and were successfully implemented, today is a group operating with fifteen breweries, six malt production facilities and a total of 3.2 billion litres of brewing capacity in five countries. Our group, initially having one brand and two packages, today has forty eight brands and around one

hundred and seventy packaging varieties. This position marks the Efes Beer Group as the sixth largest European brewer and sixteenth largest in the world.

With this occasion, I also want to underline one feature of the brewing industry that I have observed. This feature is reflected by everyone within the brewing industry including the brewers, suppliers and the sales people. In spite of competition and varying benefits, everyone in this industry is very close, open and helpful to each other. I believe this is a jubilant characteristic which is also accommodating for the industry. Throughout my thirty-four years career I gained significant experience and knowledge. You should be assured that every one of you hand an important contribution to all such values that I attained. Therefore I want you to know



there for you when you require, and to share these values with vou. Efes Beer Group was able to deliver a highly significant achievement in a comparably short duration of thirty-eight years. It is a privilege for me to have worked for and contributed to a substantial part of this accomplishment. Great achievements are reached through proper policies, faithful collaborations and important sacrifices. For that reason. I would like to thank all of you my friends and my colleagues, who also are close friends, whom I believe to have had a very important contribution to my success and the achievements of our group. I wish you all health and prosperity and hope to be together in happy and more peaceful times.

Yours sincerely.

Ahmet Boyacioglu January 30, 2007