



Peppers and their constituents against obesity

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Received: 26 February 2023 / Accepted: 17 July 2023 / Published online: 26 July 2023
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Abstract

Phytotherapy can be an efficient tool for prevention and treatment of disorders including obesity. The purpose of this narrative review is to summarize the available knowledge concerning the positive effects of peppers (*Capsicum spp.*) and their alkaloid capsaicin on human health, in particular on fat and obesity. Search for literature was performed in Medline/Pubmed, Web of Science and SCOPUS databases between the year 2000 and 2023. Words used to search were pepper, *Capsicum*, capsaicin, review, obesity, fat, weight loss and mechanisms. The available data demonstrate that both pepper extract and capsaicin can positively influence human health and treat several disorders. Moreover, they can reduce fat storage affecting brain centres responsible for the sensation of hunger, nutrient uptake by gastrointestinal tract, state of adipocytes, increase in carbohydrate and fat oxidation, metabolism and thermogenesis and other mechanisms. Therefore, despite some possible limitations, these substances could be useful for treatment of obesity.

Keywords Pepper · *Capsicum* · Capsaicin · Review · Obesity · Fat · Weight loss and mechanisms

Introduction

The most common current physiological dysfunction in the world is overweight and obesity. They can be risk factors, which facilitate diabetes mellitus and cause inflammations, cardiovascular diseases, hypertension, stroke, osteoarthritis, reproductive diseases as well as cancer. Due to the side effects of synthetic anti-obesity drugs, scientists are now focusing on natural products which produce similar effects to synthetic chemicals. One of the options to prevent and to treat these dysfunctions is application of medicinal or functional food plants or their molecules, which reduce fat accumulation and weight in a natural way (Sung et al. 2018; Azlan et al. 2022). One of such promising plant could be pepper and its alkaloids.

The aim of the present non-systematic critical review is to summarize the available knowledge concerning the positive effects of pepper (*Capsicum spp.*) and its constituents on human health, in particular on fat and obesity.

Search for literature was performed in Medline/Pubmed, Web of Science and SCOPUS databases between the year

2000 and 2023. Words used to search were pepper, *Capsicum*, capsaicin, review, obesity, fat, weight loss and mechanisms. In cases of repeated or conflicting information or references, more recent sources have been preferred.

Provenance and properties

The *Solonaceae* family comprises 20–27 *Capsicum* species, which originated in America and of which 5 are domesticated—*C. annuum* (bell pepper), *C. baccatum* (Peruvian pepper), *C. chinense* (bonnet pepper), *C. frutescens* (tabasco pepper) and *C. pubescens* (“hairy” pepper). Every species has many cultivars. The most commonly grown in Europe is hot pepper *Capsicum annuum*, which is divided into three categories: non-pungent sweet peppers, moderately pungent hot peppers and pungent (chilli) hot peppers. The other *Capsicum* species are represented by only pungent (chilli) hot pepper cultivars (Uarrota et al. 2021; Azlan et al. 2022). All contain carotenoids and phenols, vitamins C, B6 and A and minerals—iron, magnesium, phosphor, potassium and calcium. One pepper can cover the daily C vitamin requirements (Baenas et al. 2019; Azlan et al. 2022). The molecules contained in *Capsicum* have strong antioxidant properties (Srinivasan 2014). Characteristic for *Capsicum* is high content of phenylamine alkaloids—capsaicinoids (acid amides

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of C₉-C₁₁ branched-chain fatty acids and vanillylamine) and their non-pungent analogues of capsinoids. Those are the secondary metabolites of *Capsicum*, most likely intended to protect the plant from herbivores and fungi. Capsaicinoids stimulate nerve endings of receptors which recognize pain or irritation caused by chemicals or burns. Molecular foundation of capsaicinoids' effects lies in their molecular bonds to specific capsaicin TRPV1 receptors or also vanilloid receptors, which belong to the nociceptors perceiving hot taste. Vanilloid receptors function as ion channels for the entry of calcium ions into neurons and are opened by molecules of the capsaicin type or a heat stimulus. Painful burn caused by capsaicin triggers an inflammation—redness of the tissue and localised increase of temperature similar to the reaction to a light burn. At the same time, capsaicinoids and capsinoids can affect the central and peripheral sympathetic nervous system through an action on production of neuro-hormones and neuromediators (substance P, serotonin and somatostatin) (Rollyson et al. 2014; Fernandes et al. 2016; Srinivasan 2016; Varghese et al. 2017; Uarrota et al. 2021).

Capsaicinoids are the most known biologically active constituents of peppers, but the involvement of other molecules in peppers effects cannot be excluded too. One of such molecule could be the less explored capsiate, which is a non-pungent analogue of capsaicin (Gupta et al. 2022).

Positive effects on human health

Antioxidation properties of *Capsicum* molecules explain their ability to prevent mutations triggered by free radicals. Thanks to the antioxidant and anti-inflammatory properties, they are applicable in prevention and treatment of diseases caused by oxidative stress—atherosclerosis, diabetes, cataracts and tumours (Srinivasan 2014, 2016; Fernandes et al. 2016; Uarrota et al. 2021; Gupta et al. 2022; Wang et al. 2022a; Xia et al. 2023).

Their ability to activate vanilloid receptors means that capsaicinoids are able to stimulate blood circulation, increase metabolic rate and stimulate stomach secretion and therefore also digestion. It reduces acidity and increases secretion in the gastrointestinal tract, and therefore, *Capsicum* is suitable for prevention and treatment of stomach ulcers (Srinivasan 2016). It activates intracellular insulin and glucagon, decreases levels of blood sugar (Zhang et al. 2017; Uarrota et al. 2021; Wang et al. 2022b) and reduces the symptoms of metabolic syndrome and diabetes (Varghese et al. 2017; Sanati et al. 2018; Wang et al. 2022b). It improves the metabolism of carbohydrates: it redirects glycogen accumulation from the liver (where it is stored) to muscles (where it is burned) (Kim et al. 2018).

Capsaicin applied in higher doses to skin before surgeries eliminates post-operation pain. It treats neuralgic pain

in muscles and joints. Capsaicinoids have antibacterial, fungicidal and anti-inflammatory effects and therefore are also conservative. They prevent storing of cholesterol on arterial walls and damage to blood cells by cholesterol, therefore protecting the cardiovascular system (Srinivasan 2016; Cheng et al. 2023). On the capsaicinoid base, anti-inflammation medication and analgesics are being developed (Rollyson et al. 2014; Baenas et al. 2019; Wang et al. 2022a, b). These can be used to treat arthritis, neuropathic pain, dysfunctions of the digestive tract and a wide variety of tumours (Rollyson et al. 2014; Fernandes et al. 2016; Anonymous, 2021; Wang et al. 2022a; Cheng et al. 2023). For its ability to reduce pain, capsaicin has a soothing effect and improves sleep (Tremblay et al. 2016). Capsaicin can be helpful in the improvement of gut microflora (Szallasi 2022; Xia et al. 2023).

Taken together, the present general outlook of the available published data demonstrates a wide array of physiological and curative effects of peppers and its molecule capsaicin. Nevertheless, these data have some limitations, which restrict their interpretation, understanding and application. First, it remains unknown, what constituents are responsible for effects of pepper and its extract. The previous studies were focused predominantly only on capsaicinoids. Second, some effects of peppers and capsaicinoids were studied only on animals, and their anti-cancer properties were detected only on cancer cell cultures, while there is no or only few reports concerning the corresponding clinical studies. Third, the mechanisms of peppers and their constituents require further elucidation. Capsaicins can affect target cells not only via capsaicin TRPV1 and vanilloid receptors, but also via receptor-independent pathway (Srinivasan 2016), which has not been identified yet. Furthermore, capsaicins can bind reactive oxygen species and prevent oxidative stress and oxidative stress-induced inflammatory processes, as well as affect some signalling molecules like hormones and neuromediators substance P, serotonin and somatostatin (Srinivasan 2014, 2016; Azlan et al. 2022). Nevertheless, there is no sufficient evidence that these processes and molecules are really mediating capsaicins action on physiological processes and illnesses listed above.

Positive effects on weight reduction

In mice, feed containing capsaicin decreased fat storing in liver and levels of the adipose tissue hormone leptin (Seyithanoğlu et al. 2016; Wang et al. 2022b; Oh et al. 2023). *Capsicum* extract reduced their obesity and body weight (Vieira-Brock et al. 2018; Elmaz and Gezer, 2022; Wang et al. 2022b). In the experiments of Zhang et al. (2017), however, capsaicin did not reduce the body weight of rats.

In humans, regular or one-time consumption of *Capsicum annuum* red pepper or capsules with its extract led to reduced appetite for fat, savoury or sweet food (Ludy and Mattes 2011; Zanzer et al. 2018). Large-scale multicentric experiments validated that consumption of capsaicinoids reduces weight, abdominal fat stores, appetite and food consumption. Therefore, capsaicinoids can be an efficient ingredient in food with added value and food supplements applicable in programmes focused on weight reduction and improvement of metabolism (Kawabata et al. 2006; Reinbach et al. 2009; Whiting et al. 2014; Clegg et al. 2013; Varghese et al. 2017; Irandoost et al. 2021). In contrast to pepper and capsaicin, the performed clinical studies did not reveal the significant influence of non-pungent capsinoids on human weight and obesity (Marlatt and Ravussin 2017; Elmaz and Gezer, 2022; Szallasi 2022).

The ability of *Capsicum* and its molecule capsaicinoids to reduce fat stores can be explained by multiple mechanisms of action (see Elmaz and Gezer, 2022 for review):

- They modify the ultrastructure of cells of the gastrointestinal tract and increase their throughput for nutrients (Srinivasan 2016).
- They facilitate apoptosis (programmed death) of adipose cells (Lu et al. 2018), although studies (Oh et al. 2023) did not reveal the influence of red pepper leaf extracts on viability of adipocytes.
- They reduce the size of adipocytes (Mosqueda-Solís et al. 2018).
- They suppress activity of the enzymes responsible for the fat production in adipose tissue, consequently reducing the production (Lu et al. 2018; Oh et al. 2023).
- They activate conversion of white adipose tissue to brown and the enzymes responsible for oxidation and burning of fat through heat dissipation instead of its sparing in adipose tissue (Ludy and Mattes 2011; Clegg et al. 2013; Yoneshiro and Saito 2013; Gannon et al. 2016; Tremblay et al. 2016; Varghese et al. 2017; Lu et al. 2018; Silvester et al. 2019; Vieira-Brock et al. 2018; Irandoost et al. 2021)
- They promote carbohydrate and lipid oxidation (Irandoost et al. 2021)
- They stimulate release of catecholamines (metabolism activating hormones) into blood (Gannon et al. 2016)
- They improved production of insulin, which supports weight management and has positive effects in prevention and treatment of obesity (Varghese et al. 2017)
- They, via TRPV1 receptors and upregulation of intracellular calcium, affect the sympathetic nervous system (Varghese et al. 2017), and the reduced appetite after consumption of *Capsicum* molecules (Reinbach et al. 2009; Ludy and Mattes 2011; Whiting et al. 2014; Gannon et al. 2016; Tremblay et al. 2016; Zanzer et al. 2018)

indicates that these molecules can suppress the brain centre responsible for the sensation of hunger

- Pepper can downregulate adenosine 5'-monophosphate-activated protein kinase (AMPK), which promotes production of adiponectin and its receptor, which in turn promotes fat storage (Wang et al. 2022b).
- Capsaicin can have an indirect effect through its ability to reduce pain, to soothe, improve sleep and consequently reduce food consumption (Treamblay et al. 2016).

Therefore, the ability of pepper extracts and capsaicin to induce weight loss via several extra- and intracellular mechanisms is documented.

On the other hand, the current knowledge concerning anti-obesity action of pepper has even more limitations that evidence concerning its general health effect listed above.

Some reported data are contradictory. For example, peppers can reduce fat storage and weight loss in mice (Seyithanoğlu et al. 2016; Vieira-Brock et al. 2018) but not in rats (Zhang et al. 2017), indicating the species-specific difference in anti-obesity action of this plant. Some studies on humans demonstrated the ability of capsaicin to promote fat oxidation and thermogenesis (Yoneshiro and Saito 2013; Gannon et al. 2016; Irandoost et al. 2021), but some similar human studies does not detect such effects (Schwarz et al. 2013). It is proposed (Yoneshiro and Saito 2013) that capsaicin can induce thermogenesis only in subjects with developed brown adipose tissue. This fact doesn't correspond to the hypothesis that capsaicin induces fat browning (Silvester et al. 2019). Moreover, it can limit capsaicin applicability as anti-obesity drug in human medicine. Treatments of either laboratory rodents or humans with capsinoids, the non-pungent analogues of capsaicin, were able to induce energy expenditure through thermogenesis, but it did not affect fat storage and weight loss (Marlatt and Ravussin 2017). These observations suggest that the anti-obesity action of pepper molecules capsaicin and capsinoids is not due to their action on thermogenesis.

The majority of the reported clinical studies examined the anti-obesity action of capsaicin and capsaicinoids, but not of natural food peppers (Gannon et al. 2016; Irandoost et al. 2021), although peppers, in comparison to capsaicin and capsainoids, can be more natural and cheap nutrient containing several anti-obesity molecules. It still remains to be established, whether peppers action on fat storage and metabolism is defined by the presence of only capsaicin. The analysis of the available publications indicates not only similarity, but also some differences between pepper extract and capsaicin action, while to our knowledge their effects have not been compared in the same experiments. Such differences could be due to the presence of anti-obesity molecules others than capsaicin. For example, vitamins C (Garcia-Diaz et al. 2014), A (Blaner 2019) and B6 (Bird 2018) possess

anti-oxidant, anti-inflammatory and anti-obesity activities like capsaicin. The anti-oxidant and anti-inflammatory action of these vitamins might explain their anti-obesity effects, but the mechanisms of these effects require further studies.

Even the mechanisms of action of capsaicin are studied insufficiently. For example, the hierarchical functional interrelationships between capsaicin mediators listed above are not to be excluded. Nevertheless, to our knowledge, the corresponding profound studies aiming to understand these interrelationships have not been performed yet.

Possible adverse side effects

Regular consumption of red pepper reduced its effect due to habit formation (Ludy et al. 2011). At the same time, *Capsicum* or capsaicinoids can sometimes cause irritation of intestines or skin. They can also increase the risk of bleeding; therefore, patients who take blood-thinning medication should be very cautious. They can trigger reaction in people allergic to plants from the *Solanaceae* family or suffering from asthma (Anonymous, 2021; Chang et al. 2023). Long-term consumption of capsaicin in large (over 100 mg/kg body weight) doses can cause stomach ulcers and facilitate occurrence of prostate, duodenum and liver cancer and metastases in breast cancer (Rollyson et al. 2014). Two occurrences of heart attack have been reported in patients taking cayenne pepper pills (Sayin et al. 2012; Akçay et al. 2017), but direct causation was not proven. Regardless of these incidents, the U.S. Food and Drug Administration generally considers *Capsicum*-based food supplements and medication safe and does not require special permits for their production and application (Anonymous, 2021). Therefore, peppers can be considered as relatively safe functional food with anti-obesity effect.

Conclusions for future biology

Extracts and components of *Capsicum* can have positive effects in prevention and treatment of multiple diseases. Experiments on animals and clinical tests demonstrated the positive effects on food intake, production and storing of fat, whereby these are performed on multiple levels of regulation. Conclusively validated were the applicability of *Capsicum* extract and its components to reduce body weight in healthy people as well as people with excess weight. Despite possible health risks, *Capsicum* is considered a safe and efficient method to suppress appetite and stimulate weight loss. It can be efficient in long-term (more than 12 weeks) as well as short-term (even one-time) application. Therefore, the use

Capsicum and its molecules to stimulate weight loss can be recommended.

The question of how to use of them has a more complicated answer. Individual tolerance to capsaicinoids can be an issue. According to the results of research, daily doses of these molecules stimulating weight loss in humans were 2 mg to 10 g (in animals as much as 100 g). Capsaicinoids, however, are responsible for the hot taste of *Capsicum* and act on taste receptors at already extremely low doses. Lovers of hot food will enjoy this treatment. However, for other people consumption of hot preparations at this dosage may be unbearable. For those, less hot but just as biologically efficient pills and beverages are being tested (Kawabata et al. 2006; Rollyson et al. 2014; Gannon et al. 2016; Zanzer et al. 2018; Baenas et al. 2019). Capsaicinoids cannot be a non-pungent alternative to peppers and capsaicin at least for weight loss because their anti-obesity effect has not been demonstrated yet (Marlatt and Ravussin 2017).

The non-pungent alternative to hot peppers and their capsaicinoids could be sweet peppers containing capsiate, a non-pungent analogue of capsaicin. It possesses relatively low toxicity and the ability to reduce weight loss (Gupta et al. 2022).

Taken together, the data summarized here suggest that peppers, capsaicinoids and maybe some their non-pungent analogues and constituents can be an efficient tool for improving health state, fat metabolism and body weight.

Acknowledgements This manuscript had no funding.

Author contributions This manuscript was generated by one person—AVS.

Funding Open access funding provided by The Ministry of Education, Science, Research and Sport of the Slovak Republic in cooperation with Centre for Scientific and Technical Information of the Slovak Republic.

Data availability The data will be provided on request.

Declarations

Conflict of interest The author declares no conflict of interest. He wishes to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Ethical approval The present study was performed according to international, national and institutional rules considering animal experiments, clinical studies and biodiversity rights. The present publication reviews the data published previously; therefore, the restrictions concerning animal experiments and clinical studies are not applicable here.

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