Further research on the biological activities and the safety of raspberry ketone is needed

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1. Introduction

Until recently, raspberry ketone (also known as 4-(p-hydroxyphenyl)-2-butanone, 4-(p-hydroxyphenyl)-2-butanone, 4-(4'-hydroxyphenyl)-2-butanone, p-hydroxybenzyl acetone, and frambinone; Fig. 1) had mostly been an ingredient for the flavor and fragrance industry [1]. That changed in 2012 after claims of it having anti-obesity activity were made in US media [2], once again bringing the prospect of a miracle pill that will keep you slim. From North America to East Asia, popular US TV programs sway consumer purchasing with features on dietary products that suggest that consumption of their supplements offers improved health benefits [2]. Unfortunately for the widespread viewing audiences, the desire to overcome disease or just to lose weight makes it easy for them to believe in exaggerated health claims and seek out the next miracle pill/drug [2]. Dietary supplements containing raspberry ketone are one of the latest products in this optimistic spotlight.

Raspberry ketone is a volatile phenolic compound (Fig. 1) and only one component of the complex mixture of raspberry fruit volatiles (esters, aldehydes, alcohols, terpenes, terpenoids, ketones, pyrazines, etc.) that together make what we associate as natural raspberry fruit aroma [1-14]. The amount and types of raspberry volatiles found in the fruit may change between harvest and final commercial products with processing conditions, storage environment, or time. [6,7,15]. For example, one study reported raspberry volatile concentrations to have been unchanged after a one-year of frozen storage (eight compounds monitored) [6], while another [7] saw changes immediately after deep-freezing of samples (75 compounds monitored), although these two studies examined different collections of volatiles.

Raspberry ketone was discovered in 1903, and its chemical structure was first identified in 1951 from raspberries [16]. Within the raspberry plant it is biosynthesized via the phenylpropanoid pathway, like other phenolic compounds [13,17]. Pure raspberry ketone is a powder of translucent white, short needle-shaped crystals, and considered the main constituent of raspberry aroma [1]. It has a low human odor threshold of 0.001 to 0.1 mg/kg [10], and been described as having a "raspberry", "sweet", "perfume", "woody", and "hot tea" aroma and taste [8,9,15], although others report it having a slightly different smell from natural ripe raspberry fruit [18]. Raspberry fruit volatiles and their sensory perceptions were recently well reviewed previously [19].

There are numerous species of raspberries [20], but when raspberry ketone is typically mentioned in popular media (or the literature) it’s in reference to red raspberry (Rubus idaeus L.), and for clarification, unless indicated otherwise, all raspberry mentioned in this review refers to red raspberry. The objective of this review was to summarize past scientific findings to educate researchers, medical professionals, and consumers regarding raspberry ketone.

2. Raspberry ketone concentrations and role in nature

Natural raspberry ketone has been found to range from 0.001 to 4.2 mg/kg in raspberry juices and pulps, from wild genotypes and a...
variety of cultivars (Table 1) [4,7,9,10,13]. The variations in concentrations reported have been directly attributed to fruit being wild collected versus cultivated, cultivar differences, genotypes, environments, or growing seasons, and indirectly due to sample forms, sample preparation prior to analyses, and analytical methods used [4,7,13,14,19].

Although raspberry ketone’s exact role within the plant is yet to be determined, it is thought to be an insect kairomone or synomone [21, 22], and has been used as an ingredient in insect baits [23,24]. General information about possible roles of plant volatiles has been well reviewed [25,26]. Raspberry ketone also has some antifungal capacity as well [1,27].

3. Raspberry ketone sources

Raspberry ketone is not unique to raspberries and has been found in baby kiwi (Actinidia arguta Planch. ex Miq.) [28], brewed coffee [29,30], yew (Taxus baccata L.) [31,32], and orchid flowers (floral lip part; Bulbophyllum apertum) [21] with concentrations ranging from 0.00081 to 4.2 mg/kg (Table 1). European cranberry (Vaccinium oxycoccus L.), and lingonberry (V. vitis-idea L.; also known as cowberry) have been reported to contain raspberry ketone as well, although Honkanen et al. [7] cited unpublished work. Raspberry ketone is not as volatile as other groups of volatile compounds, and this may partially explain why some researchers have either reported low recovery, or not detected, when using a single sample preparation method for all volatiles of interest [8,11].

Confusingly to some consumers, perhaps due to its common chemical name including the term raspberry, this compound might be perceived as being of a natural puriﬁcation origin. Though, for the quantity of raspberry ﬂavorings needed for commercial production of food, fragrances, and cosmetics, volatiles like raspberry ketone have to be manufactured [18,33]. As very little raspberry ketone can be isolated from natural sources due to its low concentration concentrations (Table 1), for its use in the majority of products it is synthesized, either chemically [34], by tissue culture [18,35,51], or by biotransformation/bioconversion (chemically or enzymatically) [17,34,36,37]. The history of how raspberry ketone became synthetically produced in sufﬁcient amounts to supply the baking, cosmetic, and beverage industries was well summarized previously [18,33,34].

Raspberry ketone has held GRAS (Generally Recognized as Safe; 21CFR172.515) status since 1965 [1] as an ingredient for use in a food, drug, or cosmetic and is listed under synthetic ﬂavoring substances with the instruction to use minimum quantity that produces intended effect. According to Code of Federal Regulations (21CFR101.22) definitions, “natural ﬂavor/ ﬂavoring” compounds have to be extracted from a plant or substance listed in 21CFR172.510. So, by that deﬁnition most (or all) commercially available raspberry ketone would not be considered natural, but rather a synthetic ﬂavoring (21CFR172.515) [38]. The European legal deﬁnition for “natural” ﬂavoring is even stricter than that of the US [39] regarding manufacturing process to obtain ﬂavoring compounds. A stable isotope ratio comparison technique for identifying the authenticity of (natural versus synthesized) raspberry aromas like α-ionone, β-ionone, and α-ionol has been demonstrated, but its ability to distinguish natural raspberry ketone from synthetic has not been shown yet [39].
The US Government Accountability Office (GAO) published over 3500 cases of general dietary supplement adverse event that they recorded for the years 2003 to 2008, ranging from non-serious injuries/illness to disability, life threatening, and death [47]. Although specific adverse events attributed to raspberry ketone have not surfaced yet, the fact that it has not demonstrated treatment efficacy and no safety data warrant caution in its use as a treatment for any condition.

5. Concluding remarks

There is insufficient scientific evidence that raspberry ketone can aid the fight against human obesity. Additional work is clearly needed, and until then raspberry ketone dietary supplements should be consumed with restraint. Because US dietary supplements are able to make unsubstantiated health claims and the difficulty for consumers to be sure of product authenticity, nutrition obtained from whole food forms is likely the safer and less expensive way to obtain these compounds. Raspberry fruit contains other macro- and micronutrients (fiber, vitamins, etc.) that are also important in a healthy diet, all well reviewed before [48, 49]. As we’ve previously done [20,50], we continue our efforts to educate researchers, medical professionals, growers, and consumers about misconceptions in popular media and scientific reality regarding Rubus fruit, their metabolites, and human health.

Conflict of interest

None.

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References


