Raspberry Ketone: A Natural Preservative Booster for Oral Care Products

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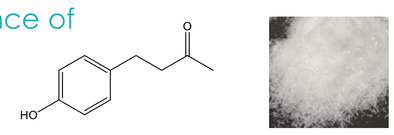
abstract #3571457

A natural phenolic compound found in red raspberries and other fruit, raspberry ketone acts synergistically with antimicrobial actives, commonly used in oral care, against the dental carries causing pathogen, *Streptococcus mutans.* In addition, raspberry ketone was shown to act as preservative booster in a mouthwash formulation.

introduction

Raspberry ketone (R-K) is a naturally occurring product that has been used for decades in traditional Chinese medicine and Ayurvedic traditions. It is part of a family of compounds known as phenylpropanoids, which also include green tea catechins and benzoic acid and are known to protect against microorganisms. Raspberry ketone occurs as snowy white crystals with a neutral to faint raspberry taste.

Structure and appearance of raspberry ketone



Oral pathogens are responsible for multiple medical conditions including dental caries, halitosis and gingivitis. Synergistically acting antimicrobial combinations can act as multiple-hurdles for controlling microorganisms. This approach can lead to a number of benefits such as reducing the total concentration of actives in a formulation, the ability to modulate the antibacterial spectrum of the actives and minimization of adaptive mutations.

In addition, many oral care formulations, including fluoride mouth washes are formulated at close to neutral pH, and can be challenging to preserve. Raspberry ketone can boost the activity of commonly used preservatives which can lead to a reduction of preservative levels needed for adequate preservation.

methods

Interactions between raspberry ketone and other antimicrobials were evaluated using standard checkerboard assay described by Kull A.C. et al[1].

To determine antimicrobial synergy, Synergy Index (SI) was calculated using the following equation:
SI = Qa/QA + Qb/QB, where:

- Qa and Qb represent concentrations (in ppm) of compound's A and B in the combination being evaluated
- QA and QB represent the individual Minimal Inhibitory Concentrations (MICs) in ppm of compound's A and B

Preservative efficacy testing (PET) was done following a modified Personal Care Products Council (PCPC) protocol in an alcohol-free, neutral pH mouthwash base. The samples were challenged with six microorganisms: *S. aureus*, *E. coli*, *B. cepacian*, *P. aeruginosa*, *C. albicans* and *A. brasiliensis*. Surviving microorganisms were enumerated after 2, 7 and 14-days of incubation at 28° C using the pour-plating method.

Mouthwash formulas for preservative efficacy testing

Ingredient	1 % (w/w)	2 % (w/w)	3 % (w/w)	4 % (w/w)
Cetylpyridinium chloride (CPC)	0.00	0.00	0.020	0.020
Raspberry ketone (R-K)	0.00	0.500	0.00	0.500
Water	73.63	73.13	73.61	73.11
Sorbitol 70% solution	15.00			
Propylene glycol	8.00			
Poloxamer 407	3.00			
Polysorbate 20	0.06			
Sodium fluoride	0.05			
Menthol	0.04			
Methyl salicylate	0.04			
$Na_2HPO_4 \cdot 2H_2O$	0.063			
$NaH_2PO_4 \cdot H_2O$	0.038			
Sodium saccharin	0.038			
Peppermint flavor oil	0.038			
Total	100.0	100.0	100.0	100.0
pH (as-is)	6.8			

results

Table 1. Raspberry ketone acts synergistically with commonly used oral care antibacterial agents against *S. mutans*

oral care active	Qa active conc. (ppm)	Qb Raspberry ketone conc. (ppm)	Synergy index (SI)*
isopropyl methylphenol (IPMP)	250	125	≤0.5016
thymol	15.6	4,000	≤0.625
menthol	1,000	4,000	≤0.75
chlorhexidine digluconate	0.4	4,000	≤0.75
cetylpyridinium chloride monohydrate (CPC)	0.3	2,000	≤0.75

* SI <1 indicates synergistic antimicrobial effect. The lower the SI index the greater the synergy.

Table 2. Raspberry ketone acts synergistically with antimicrobials commonly used for preservation of personal care products

antimicrobial	Synergy index * for antimicrobial interactions with raspberry ketone versus common microbial contaminants		
	S. aureus	*B. cepacia*	*A. brasiliensis*
benzyl alcohol	≤0.625	1	0.75
phenethyl alcohol	≤0.750	0.625	1
phenyl propanol	≤0.5625	0.75	1
tetradecyl trimethyl ammonium bromide	≤0.500	0.625	0.325
caprylhydroxamic acid	≤0.625	0.75	0.5625

Table 3. Raspberry ketone shows preservative boosting effect in an alcohol-free, fluoride mouthwash

formulation	Micro-organisms	2 days	7 days	14 days
(1) mouthwash (m/w) base	Bacteria	5.11E+05	1.06E+03	<10
	Fungi	2.60E+05	1.50E+05	4.10E+04
(2) m/w base+ 0.5% R-K	Bacteria	2.00E+01	<10	<10
	Fungi	1.50E+04	3.50E+04	5.00E+03
(3) m/w base+ CPC	Bacteria	<10	<10	10
	Fungi	5.00E+01	1.00E+01	1.00E+01
(4) m/w base+0.5% R-K & CPC	Bacteria	<10	<10	<10
	Fungi	<10	<10	<10

conclusions

- Raspberry ketone, a natural compound, acts synergistically with common oral care antimicrobial agents against *S. mutans.*
- The use of raspberry ketone in a formulation can boost the activity of commonly used preservatives needed for microbial safety of the product.

references

1. Kull A.C., Eisman, P.C. Sylwestowicz, H.D. and Mayer, R.L. 1961. Applied Microbiology, 9:538-541

Ashland is the supplier of the raspberry ketone compound tested herein

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