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Subject: Raspberry ketone

Posted by [Hammerhaar](#) on Wed, 12 Mar 2008 15:34:02 GMT

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Die Studie ist glaube ich noch nicht gepostet worden:

Effect of topical application of raspberry ketone on dermal production of insulin-like growth factor-I in mice and on hair growth and skin elasticity in humans.

Harada N, Okajima K, Narimatsu N, Kurihara H, Nakagata N.

Department of Translational Medical Science Research, Nagoya City University Graduate School of Medical Sciences, Kawasumi 1, Mizuho-cho, Mizuho-ku, Nagoya 467-8601, Japan.

Sensory neurons release calcitonin gene-related peptide (CGRP) on activation. We recently reported that topical application of capsaicin increases facial skin elasticity and promotes hair growth by increasing dermal insulin-like growth factor-I (IGF-I) production through activation of sensory neurons in mice and humans. Raspberry ketone (RK), a major aromatic compound contained in red raspberries (*Rubus idaeus*), has a structure similar to that of capsaicin. Thus, it is possible that RK activates sensory neurons, thereby increasing skin elasticity and promoting hair growth by increasing dermal IGF-I production. In the present study, we examined this possibility in mice and humans. RK, at concentrations higher than 1µM, significantly increased CGRP release from dorsal root ganglion neurons (DRG) isolated from wild-type (WT) mice and this increase was completely reversed by capsazepine, an inhibitor of vanilloid receptor-1 activation. Topical application of 0.01% RK increased dermal IGF-I levels at 30min after application in WT mice, but not in CGRP-knockout mice. Topical application of 0.01% RK increased immunohistochemical expression of IGF-I at dermal papillae in hair follicles and promoted hair re-growth in WT mice at 4 weeks after the application. When applied topically to the scalp and facial skin, 0.01% RK promoted hair growth in 50.0% of humans with alopecia (n=10) at 5 months after application and increased cheek skin elasticity at 2 weeks after application in 5 females (p<0.04). These observations strongly suggest that RK might increase dermal IGF-I production through sensory neuron activation, thereby promoting hair growth and increasing skin elasticity.

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Subject: Re: Raspberry ketone

Posted by [Hammerhaar](#) on Wed, 12 Mar 2008 15:35:48 GMT

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Die Frage ist, ob es wirklich was bringt, wenn ja, woher man das bekommen kann und wie die Lösung zusammengesetzt sein müsste.

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Subject: Re: Raspberry ketone

Posted by [Hammerhaar](#) on Mon, 17 Mar 2008 15:14:47 GMT

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Hm....

interessiert wohl niemanden...

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Subject: Re: Raspberry ketone  
Posted by [1234567](#) on Mon, 17 Mar 2008 15:19:42 GMT  
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Hammerhaar schrieb am Mon, 17 März 2008 16:14Hm....  
interessiert wohl niemanden...

doooooooooch aber ist englisch

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Subject: Re: Raspberry ketone  
Posted by [Hammerhaar](#) on Mon, 17 Mar 2008 15:47:07 GMT  
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Also:

Himbeerketon (von der Struktur dem Capsaicin ähnlich) führt bei Mäusen zu einer Erhöhung von IGF-I in der Haut.  
Bei Menschen konnte man nach fünf Monaten eine höhere Elastizität der Gesichtshaut und bei 50% der Anwender mit Alopezie Haarwuchs beobachten.

Weiß aber nicht, ob das wirklich aussagekräftig ist, denn n=10 heisst doch wohl, dass es nur 10 Versuchspersonen gab, oder?

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Subject: Re: Raspberry ketone  
Posted by [pippo24](#) on Mon, 24 Mar 2008 13:47:53 GMT  
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das problem ist das es nur in ganz bestimmten % dosierungen die gewünschten effekte bringt.Zuviel davon ist nutzlos und soweit ich gesehen habe ist das vehicle das die verwendet haben ein schlechter penetratator dh. wenn man noch andere topicals verwendet dann kalppt es auch nicht mehr...  
Aber ansich scdhon interessant.

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Subject: Re: Raspberry ketone  
Posted by [Hammerhaar](#) on Mon, 24 Mar 2008 16:17:56 GMT  
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Übers Vehikel hab ich nichts gefunden--  
Wo hast du das gelesen, Pippo?

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Subject: Re: Raspberry ketone  
Posted by [pippo24](#) on Mon, 24 Mar 2008 20:14:11 GMT  
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Hier von HLT: Einer hat die discssion von der studie hochgeladen

I was trying to upload the study to HLT but 200K is the max file size limit. Here is the Discussion portion.. btw, the only mention of a vehicle consisted of RK being dissolved in 10% Tween 20/10% ethanol (10%) and diluted with normal saline. Also, 0.01% had the most positive effects on IGF-I levels so that's the ideal concentration. (Polysorbate 20 = Tween 20)

#### Discussion

In the present study, we examined whether RK activates sensory neurons, thereby increasing CGRP release from sensory neurons isolated from WT mice. Since the structure of RK is quite similar to that of capsaicin, it is possible that RK activates sensory neurons by activating VR-1. Consistent with this hypothesis are observations in the present study demonstrating that RK, at concentrations higher than 1 $\mu$ M, increased CGRP release from DRG isolated from WT mice and that this increase was completely reversed by CPZ, an inhibitor of VR-1 activation.

We previously reported that activation of sensory neurons by topical application of capsaicin increases dermal IGF-I production in WT mice [15], suggesting that topical application of RK might increase dermal

IGF-I levels by activating sensory neurons in WT mice. Consistent with this hypothesis are observations in the present study showing that topical application of 0.005% and 0.01% RK increased dermal IGF-I levels in WT mice, but not in CGRP<sup>-/-</sup> mice at 30 min after topical application. Since skin fibroblasts have been shown to express the CGRP receptor [24] and are capable of producing IGF-I [8], our present observations suggest that topical application of 0.01% RK might increase dermal IGF-I levels in skin fibroblasts through activation of sensory neurons.

Although RK increased CGRP release from DRG isolated from WT mice in a concentration dependent manner in vitro, RK, at concentrations higher than 0.05%, did not increase dermal IGF-I levels in these mice at 30 min after topical application. We previously reported that dermal IGF-I levels increased transiently after topical application of 0.01% capsaicin in WT mice [15]. Preliminary experiments showed that, although dermal IGF-I levels at 30 min after topical application of 0.05% and 0.1% capsaicin were significantly lower than those after topical application of 0.01% capsaicin, at 15 min after 0.05% and 0.1% capsaicin application, these levels were significantly higher than those after 0.01% capsaicin. These observations suggest that 0.05% and 0.1% RK might more strongly stimulate sensory neurons than 0.005% and 0.01% RK, thereby rapidly increasing dermal IGF-I levels with peak time points earlier than 30

min after topical application and that these increases might be followed by a rapid decrease due to depletion of CGRP from sensory neurons. Consistent with this hypothesis are observations made in the present study demonstrating that RK concentrations in the skin at 30 min after topical application of 0.1% RK were 10 times higher than those after 0.01% RK application. Thus, excessive stimulation of sensory neurons by high concentrations of RK might explain why 0.01% RK increased dermal IGF-I levels, while neither 0.05% nor 0.1% RK had this effect 30 min after topical application as shown in the present study. This possibility should be further investigated.

Topical application of 0.01% RK increased dermal IGF-I levels at 30 min after application as shown in the present study. Production of IGF-I via capsaicin *in vivo* is more rapid than that occurring in response to CGRP *in vitro* [25], indicating that the former might not be mediated by the increase in transcription as in the latter, but rather by other unknown mechanism(s). Our previous report demonstrated that subcutaneous administration of capsaicin increased tissue levels of IGF-I and IGF-I mRNA in various organs including the skin at 30 min after administration in mice [14], raising the possibility that stimulation of sensory neurons by topical application of 0.01% RK might increase IGF-I production by increasing its transcription. This possibility should be examined in future experiments.

In the present study, immunohistochemical expression of IGF-I at dermal papillae in hair follicles is clearly increased in WT mice to which 0.01% RK had been topically applied for 4 weeks as shown in the present study. Consistent with these observations is a previous report demonstrating that IGF-I is produced by dermal papilla cells [7]. IGF-I is known to be an important growth factor in many biological systems [26] and it has also been shown to play a critical role in promoting hair growth [4]. Since IGF-I receptor mRNA was detected in keratinocytes [8], it is possible that IGF-I produced by dermal papilla cells acts on keratinocytes, thereby promoting hair growth through stimulation of the proliferation of keratinocytes in hair follicles [4]. Thus, it is possible that increase in IGF-I levels in hair follicles with topical application of 0.01% RK promotes hair growth in WT mice. Consistent with this hypothesis are our present observations demonstrating that hair re-growth was more marked in WT mice to which 0.01% RK had been topically applied for 4 weeks than in those receiving vehicles for 4 weeks.

In contrast to our results, capsaicin has been shown to inhibit hair shaft elongation by inducing premature hair follicle regression via VR-1 stimulation of the outer root sheath keratinocytes in organ-cultured human scalp hair follicles [27]. However, in the present study, RK significantly increased IGF-I expression and promoted hair re-growth in mice. These observations suggest that RK might interact mainly with VR-1 on sensory neurons, thereby increasing IGF-I production in dermal papillae through an increase in CGRP release from sensory neurons *in vivo*.

Topical application of 0.01% RK to the scalp for 5 months promoted hair growth in 5 of the 10 volunteers with alopecia in the present study. Consistent with these observations is our recent report demonstrating that administration of capsaicin and isoflavone promoted hair growth by increasing IGF-I production in humans with alopecia [19]. These observations raised the possibility that topical application of 0.01% RK to the scalp increases IGF-I production in hair follicles through activation of sensory neurons, thereby promoting hair growth in humans

suffering from alopecia. These possibilities should be further examined in a large controlled study of human subjects with alopecia.

We previously demonstrated that stimulation of sensory neurons increases tissue blood flow by increasing endothelial productions of nitric oxide and prostacyclin through activation of endothelial nitric oxide synthase and cyclooxygenase-1, respectively [28]. Thus, it is possible that stimulation of sensory neurons by RK increases dermal blood flow, thereby contributing to the promotion of hair growth. Furthermore, capsaicin has been shown to down-regulate androgen receptor expression by prostate cancer cells [29]. Since androgen plays a critical role in the development of alopecia [30] and balding hair follicle dermal papilla cells contain higher levels of androgen receptors than those from non-balding scalp [31], RK, like capsaicin, might promote hair growth by decreasing androgen action through androgen receptor down-regulation on dermal papilla cells.

CGRP has been shown to promote proliferation of human keratinocytes by increasing intracellular cAMP levels in vitro [32], suggesting that topical application of 0.01% RK might promote hair growth not only by increasing IGF-I production, but also by increasing CGRP release from sensory neurons in mice and humans with alopecia.

IGF-I increases the production of collagen [10] and elastin [33] by skin fibroblasts and promotes proliferation of keratinocytes [34], suggesting that IGF-I produced by fibroblasts might act on these fibroblasts themselves as well as on keratinocytes, thereby promoting the productions of both collagen and elastin as well as proliferation, respectively. Patients with Laron syndrome showed skin morphological changes such as decreased thickness with decreased elastin contents [35]. The IGF-I receptor has been demonstrated in human skin biopsies [8]. These observations suggest that detrimental skin morphological changes observed in patients with Laron syndrome might be attributable to reduced production of IGF-I.

Topical application of 0.01% RK to facial skin significantly increased cheek skin elasticity in 5 healthy female volunteers after 14 days of application ( $p < 0.04$ ). Consistent with these observations is our previous report [15] demonstrating that topical application of 0.01% capsaicin to facial skin increased cheek skin elasticity in female volunteers. The important mechanical property that primarily maintains skin elasticity is attributable to the content and molecular structure of collagen fibers embedded in the ground substance [36]. The sweat secretion rate has been found to be decreased in patients with GH deficiency who have low serum IGF-I levels [37]. Decreased ability to sweat results from the atrophy of eccrine sweat glands due to lack of stimulation by either GH or IGF-I, or both [38]. Since intra-epidermal elasticity is known to be associated with the presence of sweat [39], topical application of 0.01% RK might have increased sweat in the facial skin epidermis of the volunteers, thereby contributing to the increase in facial skin elasticity.

Detrimental skin morphological changes such as decreases in skin thickness and collagen contents are observed in postmenopausal women [40] as well as in patients with Laron syndrome [35], raising the possibility that topical application of 0.01% RK might increase



skin elasticity, probably by increasing dermal IGF-I contents in aged women.

Hier mal bilder:

Thus, excessive stimulation of sensory neurons by high concentrations of RK might explain why 0.01% RK increased dermal IGF-I levels, while neither 0.05% nor 0.1% RK had this effect 30 min after topical application as shown in the present study.

## File Attachments

1) [ddgxuh.jpg](#), downloaded 1223 times

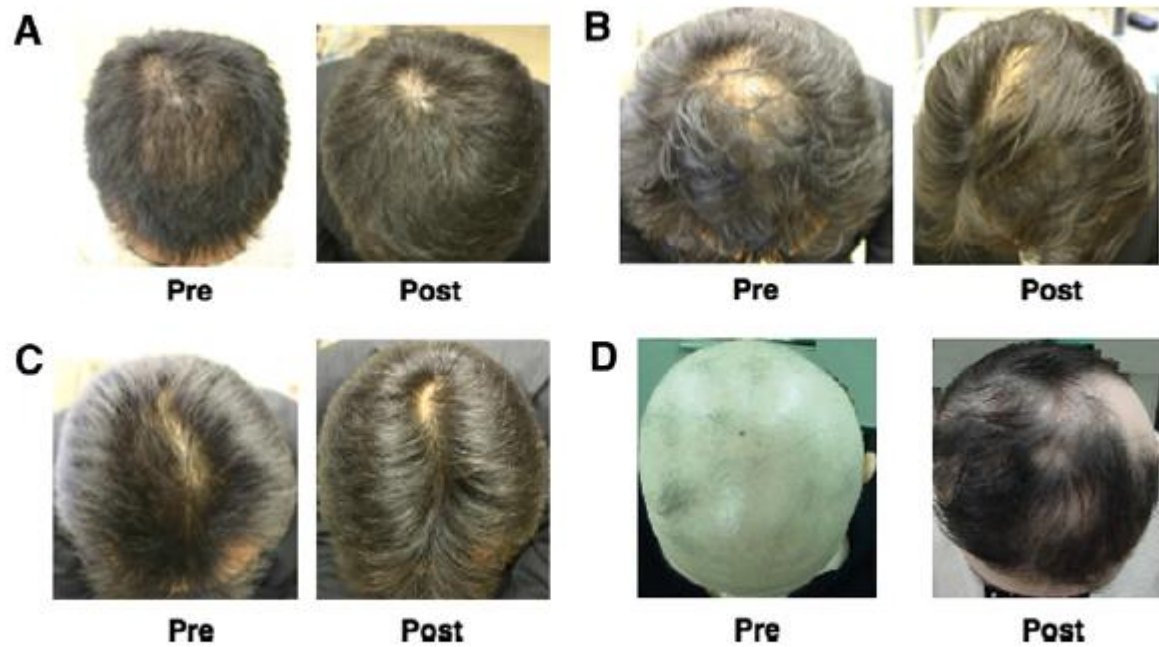
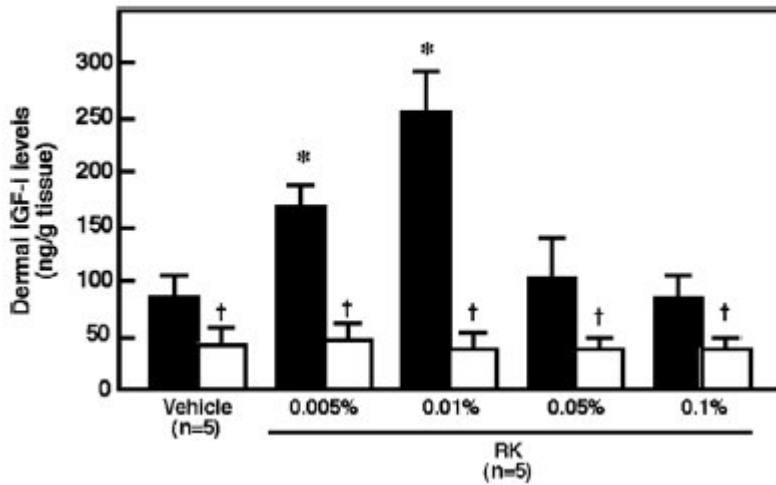


Fig. 7. Effect of topical application of RK on hair growth in volunteers with alopecia. Hair growth was observed at 5 application of 0.01% RK in 3 males volunteer with AGA (A, 30 years old; B, 28 years old; C, 36 years old) and in a female volunteer (D, 45 years old).

2) [zlvoye.jpg](#), downloaded 1208 times




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Subject: Re: Raspberry ketone  
 Posted by [stealth](#) on Fri, 11 Apr 2008 17:31:46 GMT  
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doch,mich.  
 hat parker nicht mal gepostet IGF-1 ist  
 schlecht?weiß nimmer genau.  
 denke aber das in ähnlichen beeren das gleiche drin ist.  
 hat tricomin bei dir was sichtbares gebracht,bzw.kannst  
 du es weiterempfehlen?  
 hältst du auch den 3std.abstand bei revivo ein?  
 schon wirkung?  
 obwohl bei deinen vielen medis wahrsch.ein bestimmtes  
 medi schwer rauszupinnen ist.  
 erzähl doch mal  
 b.g.  
 STEALTH

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Subject: Re: Raspberry ketone  
 Posted by [stealth](#) on Fri, 11 Apr 2008 17:38:06 GMT  
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dann hat capsaicin also  
 eher negative wirkung,laut studie sogar ganz deutlich.  
 check this,methode24  
 b.g.  
 STEALTH

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Subject: Re: Raspberry ketone  
Posted by [ParkerLewis](#) on Fri, 11 Apr 2008 18:26:29 GMT  
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stealth schrieb am Fre, 11 April 2008 19:31 doch, mich.  
hat parker nicht mal gepostet IGF-1 ist  
schlecht? weiß nimmer genau.  
denke aber das in ähnlichen beeren das gleiche drin ist.  
hat tricomin bei dir was sichtbares gebracht, bzw. kannst  
du es weiterempfehlen?  
hältst du auch den 3std.abstand bei revivo ein?  
schon wirkung?  
obwohl bei deinen vielen medis wahrsch. ein bestimmtes  
medi schwer rauszupinnen ist.  
erzähl doch mal  
b.g.  
STEALTH

Nicht schlecht, aber kontraproduktiv, wenn man generell einen hohen IGF-1 Spiegel hat... Und auch wenn nicht, kann es zu Nebenwirkungen kommen. Bei interner Einnahme. Ich habe mich da nur gegen das Konzept von Tino ausgesprochen... Hier geht es aber um die IGF-1 Erhöhung in der Kopfhaut, so weit ich das mitbekommen habe

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