

# Elevation of Cortisol Levels by Ingesting Liquorice

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## ABSTRACT

The effects of liquorice on the hormone cortisol are known but are not well understood. It has been noted anecdotally, but there remains little scientific literature on the link between the effects of liquorice on the body and the fact that cortisol is consistently implicated. This study demonstrates the link between liquorice and cortisol and the role that cortisol plays, together with yawning, in regulating brain temperature which is often compromised in certain neurological disorders such as multiple sclerosis. 13 volunteers aged between 21 and 28-year-old ingested liquorice as well as completing the Hospital Anxiety and Depression Scale, General Health Questionnaire, and demographic and health details. Saliva cortisol samples were collected before and after ingesting liquorice. In all cases, cortisol levels were significantly elevated after ingesting liquorice.

**Key words:** Brain Cooling, Cortisol, HPA-axis, Liquorice, Regulation, Yawning

## INTRODUCTION

The hormone cortisol has been associated with yawning and has been described in the Thompson Cortisol Hypothesis<sup>[1,2]</sup> that suggests links the rise in cortisol triggers which in turn lowers brain temperature. Threshold level rises of cortisol are proposed to be part of a complex mechanism since brain temperature can rise dramatically in people with MS<sup>[3]</sup> possibly due to excessive fatigue and irregular sleep patterns.<sup>[4]</sup> Cortisol is thought to regulate brain temperature within the hypothalamus-pituitary-adrenal (HPA)-axis,<sup>[5]</sup> which is a natural feedback loop to protect our bodies,<sup>[6]</sup> and cortisol may communicate directly with the motor cortex<sup>[7]</sup> as evidenced in mice by Hasan *et al.*<sup>[8]</sup> where sophisticated cortisol-specific receptors were involved during motor learning tasks.

Cortisol is implicated during stressful events and might be modulated by contagious yawning.<sup>[9]</sup> Curiously, the hormone is thought to rise during ingestion of liquorice because of the effects of the main ingredient, glycyrrhetic acid<sup>[10]</sup> on the

kidneys. This may be because of inhibition of the enzyme 11β-hydroxysteroid dehydrogenase type 2 which normally inactivates cortisol in the kidney. Liquorice is likely to inhibit this enzyme and so results in increases in cortisol levels.

Since the first description of side effects of liquorice,<sup>[11]</sup> some researchers have found that girls exposed to high maternal liquorice consumption through mothers during pregnancy had higher body mass index for age and reported more advanced pubertal development as compared with boys.<sup>[12]</sup> Støving *et al.*<sup>[13]</sup> suggested that increased sensitivity to glycyrrhetic acid may also arise in anorexia nervosa which may cause severe hypokalemia when combined with bizarre eating habits. Anecdotally, it would seem that people can overdose on liquorice consumption<sup>[14]</sup> which can cause rhabdomyolysis, the breakdown of skeletal muscle causing the release of myoglobin into the bloodstream.<sup>[15]</sup> Myoglobin is the protein that stores oxygen in muscles; too much myoglobin in the blood can lead to kidney damage.

Ottenbacher and Blehm<sup>[16]</sup> found that liquorice ingestion can lead to increased hypertension and others have shown

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that there may be many complications arising from liquorice consumption<sup>[17]</sup> including preterm labor,<sup>[18]</sup> and ocular complications.<sup>[19,20]</sup> The link between cortisol and yawning is now established,<sup>[1,7]</sup> and it is interesting to note that liquorice may now also play a role in creating artificially induced levels of the hormone for effects that might be used usefully for diagnosis or treatment monitoring.

## MATERIALS AND METHODS

### Participants

A total of 13 female healthy volunteers were recruited to the study aged between 21 and 28 years (mean of 23.1 years). All were students attending postgraduate courses at Bournemouth University and were approached at the end of teaching sessions. All participants were properly consented according to code of conduct and research guidelines. Exclusion criteria were chronic fatigue, congestive heart disorder, diabetes, fibromyalgia, heart condition, high blood pressure, history of stress, psychiatric disorder, hormone replacement therapy, renal problems, respiratory disorder, stroke, and food allergy including nuts and liquorice. None of the participants were on drugs containing cortisol.

### Stimuli and procedure

Saliva samples were collected before and again after ingesting a small piece of “natural liquorice” that also contained molasses syrup, wheat flour, liquorice extract, and natural flavoring (aniseed oil). The salt content was exclusively due to the presence of naturally occurring sodium (0.56 g in 100 g). Fat content was 0.4 g in 100 g, of which 0.0 g was saturated. 67 g in 100 g was carbohydrate, of which 49 g in 100 g was sugars, and 3.7 g in 100g was protein. Product brand was called “Panda” and manufactured by Orkla Confectionery and Snacks, PL 3050, 22111, Maarianhamina, Finland. Each participant ingested 8 g of “natural liquorice” with a “Manufacturing Date” of 08.05.2017 and a “Best Before Date” of 07.08.2018 which was well within the acceptable and recommended period of safe consumption.

Cortisol levels are easily detected in saliva and are a less intrusive collection method than intravenous cortisol collection. The presence of cortisol in saliva is highly correlated with blood assay,<sup>[21-23]</sup> and it is also much cheaper to analyze in the laboratory.

The Hospital Anxiety and Depression Scale (HADS),<sup>[24]</sup> General Health Questionnaire (GHQ28),<sup>[25,26]</sup> and demographic and health details were collected from all participants.

Between- and within-participants comparisons were made using t-tests in the SPSS package version 23. This enabled a comparison to be made between before and after liquorice ingestion.

### Ethics

Bournemouth University Research and Ethics approval granted: FST/17040/15.08.2017. Protective measures were put in place for collection and analysis of saliva samples; for example, disposable gloves were worn during collection and analysis. All data were coded for anonymity, confidentiality, and privacy held in a secure location. The right of participants to withdraw from the study at any time without consequences was upheld, and all saliva cortisol samples were destroyed following analysis.

## RESULTS

There were no significant differences between groups in terms of HADS anxiety and depression scores and GHQ28 scores. Normative data for saliva cortisol during midday period lie within the range: 1.2–3.0 nanograms per milliliter.

The means of the cortisol saliva 2 were higher than those of the first sample taken [Table 1] indicating higher values were reached in the second sample after ingesting liquorice. There was statistically significant difference ( $P < 0.005$ , 2-tailed) between cortisol sample 1 and 2 [Table 2].

## DISCUSSION

This study presents interesting findings in respect of cortisol elevations. The level of cortisol found in the first saliva samples was lower than that found in the second sample after participants had ingested liquorice. Furthermore, a significant difference was found between the levels of cortisol in the first sample compared with the second sample after liquorice ingestion. This concords with studies that have suggested liquorice ingestion acts on the receptors responsible for cortisol release and causes elevation in blood.<sup>[10]</sup>

Despite reports of possible side effects of liquorice ingestion in terms of its effects on body organs and functionality, it appears that it may be worthwhile investigating further this natural plant for its potential properties in affecting cortisol levels, especially in those who are affected by low cortisol production or an irregular release of the hormone, such as Cushing’s syndrome.<sup>[27]</sup>

**Table 1: Descriptive data of saliva samples**

### Paired samples statistics

Subjects	Mean	n	SD	SEM
Pair 1				
Saliva1	2.8769	13	1.12927	0.31320
Saliva2	3.9538	13	1.14936	0.31877

SD: Standard deviation, SEM: Standard error mean

**Table 2:** Comparison of Saliva Samples**Paired samples test**

Subjects	Paired differences			t	df	Sig. (2-tailed)
	Mean±SD	Std. Error Mean	95% Confidence interval of the Difference			
			Lower	Upper		
Pair 1	-1.07692±1.12706	0.31259	-1.75800	-0.39585	-3.445	12
Saliva1 - Saliva2						0.005

SD: Standard deviation

The authors acknowledge that it is a small sample study but also that it supports previous findings that indicate liquorice may be a natural product with potentially far-reaching benefit.

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