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The consumption of a Jerte Valley cherry product in humans enhances mood, and increases 5-hydroxyindoleacetic acid but reduces cortisol levels in urine

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ABSTRACT

Purpose: Jerte Valley cherries contain high levels of tryptophan, serotonin, and melatonin. These molecules have been shown to be involved in mood regulation. It has been suggested that a complex inter-relationship between brain serotonin, circulating levels of cortisol (the major stress hormone), and the hypothalamus–pituitary–adrenal axis exists in the regulation of stress responses, where cortisol and serotonin act as markers of mood disturbances. Moreover there is growing evidence that altered HPA activity is associated with various age-related pathologies. The present study evaluated the effect of the ingestion of a Jerte Valley cherry-based product, compared to a placebo product, on urine cortisol and 5-hydroxyindoleacetic acid (5-HIAA) levels, and on mood in young, middle-aged, and elderly participants.
Methods: Cortisol and 5-HIAA acid levels were measured by commercial enzyme-linked immunosorbent assay kits. The mood state profile was analysed using a visual analogue scale and the state–trait anxiety inventory.
Results: Our findings showed that the ingestion of the Jerte Valley cherry product decreased urinary cortisol and increased urinary 5-HIAA levels in all the experimental groups. Moreover, the cherry product was able to lessen anxiety status in the middle-aged and elderly participants, and enhanced subjective mood parameters, particularly family relationships in young participants, and frame of mind and fitness in both middle-aged and elderly subjects.
Conclusions: The consumption of the Jerte Valley cherry product may protect against stress and act as a mood enhancer by increasing serotonin availability to the organism, particularly with advancing age.

1. Introduction

Globally, it is estimated that as many as 450 million people suffer from mood disturbances, with depression and anxiety being among the most prevalent. As an example, 13.6% of the population in six European countries, including Spain, reported having had an anxiety disturbance during their lifetime (Alonso et al., 2004), and more than 150 million people suffer from depression at any given point in time.

The limbic hypothalamus–pituitary–adrenal (HPA) axis is a central control and regulatory system of the organism that connects the central nervous system (CNS) with the hormonal system, thereby conforming a stress-responsive neuroendocrine system (Kudielka and Kirschbaum, 2005). It is widely accepted that the activated HPA axis not only regulates body peripheral functions, but also has profound effects on the brain (Pariante and Lightman, 2008). Many patients with depressive and/or anxiety disturbances show disruptions in HPA axis reactivity as indexed by increased baseline plasma cortisol levels compared with healthy controls (Rajewska and Rybakowski, 2003; Vreeburg et al., 2009). However, not only the HPA axis, but also brain neuronal systems, including the monoaminergic systems, in particular the serotoninergic system, play an important role in the regulation of many physiological and behavioural processes including mood. In this sense, a strong relationship between the HPA axis and the serotoninergic system has been reported (Porter et al., 2004). Stress-induced elevated cortisol reduces the tonic level of serotonin in the synaptic cleft and stimulates its reuptake after a neuronal impulse, thereby leading to defective serotoninergic neurotransmission in the CNS (Tafet et al., 2001) as has been reported in depression (Duval et al., 2001).

Ageing can be defined as a progressive decline in physiological efficiency regulated by extremely complex multifactorial processes.

Abbreviations: HPA, limbic hypothalamus–pituitary–adrenal; CNS, central nervous system; aMT6-s, 6-sulfatoxymelatonin; 5-HIAA, 5-hydroxyindoleacetic acid; VAS, visual analogue scale; STAI, state–trait anxiety inventory.

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Several studies provide evidence that hyperactivity of the HPA axis contributes to the neuronal and peripheral deterioration associated with ageing (Ferrari and Magri, 2008), which is reflected in decreased concentrations of the neurotransmitter serotonin, a modulator of ageing in the brain (Sibille et al., 2007). Moreover, there is clear evidence that ageing is associated with elevated basal morning levels of circulating glucocorticoids such as cortisol (Tizabi et al., 1992). Overall, there is increasing evidence that altered HPA activity, e.g., increased glucocorticoid activity or a decreased brain serotonin concentration, is associated with several age-related pathologies (Aguilera, 2011).

The amino acid tryptophan, which is obtained from the diet in humans, is the direct precursor of serotonin. It has been shown that increases in plasma tryptophan availability enhance positive mood and dampen the cortisol response after an acute experimental stress exposure in stress-vulnerable subjects by enhancing brain serotonin mechanisms that are involved in adaptation to stress (Firk and Markus, 2009; Markus et al., 2000). For this reason, several studies have focused on evaluating the efficacy of the consumption of tryptophan-enriched diets to reduce cortisol responses and improve the ability to cope with stress, probably by way of counteracting alterations in brain serotonin (Lepage et al., 2002). However, most of these studies were carried out on animals, while available information on humans regarding the effect of tryptophan-enriched diets on both stress-induced cortisol responses and mood is scarce.

Cherries are an important source of phytochemicals and reportedly have important health-promoting properties, including antioxidant effects (McCune et al., 2011). In this regard, Jerte Valley sweet cherries contain not only high concentrations of anthocyanin pigments and phenolic compounds (González-Gómez et al., 2010), but also substantial amounts of melatonin, serotonin (González-Gomez et al., 2009), and tryptophan (Cubero et al., 2010). Also, it has been reported that both a Jerte Valley cherry-enriched diet (Garrido et al., 2010) and the ingestion of a Jerte Valley cherry-based product (Garrido et al., 2009) exhibit sleep-promoting actions, and increase both urinary 6-sulfatoxymelatonin (aMT6-s) and the antioxidant status in humans. Therefore, the purpose of this study was to compare the effect of the ingestion of a Jerte Valley cherry-based product (patent no. ES 2342141 B1), compared to a placebo product on cortisol and 5-hydroxyindoleacetic acid (5-HIAA) urinary levels and on mood, in young, middle-aged, and elderly subjects.

2. Material and methods

2.1. Participants

The study was carried out in young (20–30 years old, $n=10$; 5 men and 5 women), middle-aged (35–55 years old, $n=10$; 5 men and 5 women) and elderly (65–85 years old, $n=10$; 5 men and 5 women) volunteers whose weight, height, and body mass index (BMI) values are presented in Table 1. The study was approved by the Ethics Committee of the University of Extremadura (Badajoz, Spain) in accordance with the Declaration of Helsinki, the Council of Europe, and the Universal Declaration of UNESCO on human rights, biomedicine, and human genome. All participants were of Caucasian ethnicity and were recruited through word of mouth. There were no dropouts during the study. Each participant was ascertained to be in good health from their medical history and a clinical examination including routine laboratory tests and screening. The participants were non-smokers, were not using any medication, and abstained from alcohol. Informed consent was obtained from all participants.

2.2. Experimental design

The study had a blind, placebo-controlled, randomised, crossover design with two treatment periods of five days each, separated by a washout period of one week. Either the placebo or the Jerte Valley (Cáceres, Extremadura, Spain) cherry product was consumed twice a day, as lunch and dinner desserts. Each dose of cherry product (27.85 g) consisted of 18.85 g of pitted, freeze-dried cherries (equivalent to 141 g fresh cherries) in equal parts of four Jerte Valley cherry cultivars (Bourlat, Navalinda, Pico Negro, and Pico Colorado), plus 7.5 g maltodextrin and 1.5 g ascorbic acid (Spanish patent no. ES 2342141 B1). The freeze-dried, cherry-based product was then ground to a powder, and then diluted in water and bottled in 12 fl oz plastic bottles containing 125 ml (4.22 fl oz) of cherry-based product per dose. One dose of the product provided roughly 1580 mg phenolic compounds (expressed as gallic acid equivalents), 30 mg anthocyanins (calculated as malvidin equivalents), 690 mg total antioxidant capacity (TAC, expressed as Trolox equivalents), 2 mg tryptophan, 27 ng serotonin, and 16 ng melatonin.

The placebo was a commercial cherry-flavoured soft drink (Kool-Aid®, Kraft Foods, USA; ingredients listed: citric acid, salt, calcium phosphate, red 40, artificial flavour, ascorbic acid, artificial colour, blue 1) which was prepared by mixing it with water in the proportion recommended by the manufacturer, followed by bottling in 12 fl oz plastic bottles to contain 125 ml (4.22 fl oz) of placebo product per dose.

2.3. Cortisol and 5-hydroxyindoleacetic acid (5-HIAA) urine levels

First-void morning urine and urine at 20:00 h were collected before the trial (basal values), after a 5-day intake of the Jerte Valley cherry-based product or the placebo (trial values), and one day following its termination (post-trial values). The samples were stored at −20 °C until biochemical assay.

Cortisol levels were measured in both urine samples and 5-HIAA levels were measured in the 20:00 h urine using commercial enzyme-linked immunosorbent assay kits from DRG Diagnostics (Marburg, Germany) and IBL International (Hamburg, Germany), respectively, following the manufacturers' instructions. To adjust for variation in the dilution of urine, cortisol and 5-HIAA were expressed as urine cortisol/creatinine or urine 5-HIAA/creatinine ratios, respectively. The creatinine concentration was determined by means of the Jaffe's test.

2.4. Mood state profile

Changes in mood were measured on a visual analogue scale (VAS). These scales have been found to be effective tools in measuring changes over time in response to treatment for symptoms of mood disturbance, and their reliability and validity have been well documented (Baeken et al., 2008; McCormack et al., 1988; Mosimann et

Table 1
Weight, height, and body mass index (BMI) of young, middle-aged, and elderly participants.

	Young		Middle-aged		Elderly	
	Men	Women	Men	Women	Men	Women
Weight	81.00 ± 2.70	60.5 ± 8.22	76.00 ± 3.91	65.2 ± 4.54	77 ± 9.62	64.33 ± 9.13
Height	1.80 ± 0.04	1.61 ± 0.02	1.74 ± 0.06	1.65 ± 0.03	1.75 ± 0.01	1.61 ± 0.05
BMI	24.86 ± 0.68	23.07 ± 2.57	24.89 ± 0.78	23.84 ± 2.54	24.97 ± 2.84	24.76 ± 2.88

Each value represents the mean ± SD of five participants.