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Salt: a matter of balance

Once upon a time, an ancient king tried to find out which of his three daughters was most deserving of his kingdom. He called for the three princesses and asked them how much they loved him. While the oldest replied that she loved him as much as she loved pearls and precious stones, the middle daughter compared her love for him to her love of the sun light. Very pleased, he waited for the reply of his secret favourite, the youngest. When she compared her love for him to the love of the people for salt, the hurt and disappointed king exiled her from her home. Later, as the story goes, she secretly returns to the palace as a cook, and it takes just one beautifully prepared and decorated, but unsalted meal for the king to realize who of the three was most deserving of becoming the queen of his lands.

Chemically, ionic compounds that result from the neutralization reaction of an acid and a base are referred to as salts; however, in everyday terms, salt usually refers to sodium chloride, which plays a prominent role in human physiology as the main electrolyte component of the extracellular fluid and main factor of osmotic regulation.

For millennia, salt was so difficult to find and obtain that it was highly valued to the point of being used as a currency in antiquity. 'You are the salt of the earth' Jesus says in Matthew 5:13, and historians trace back the origin of words such as salad (vegetables with salt on them) or salary (paid to the Roman military in form of the precious compound) to this highly valued ionic compound. Even today, English town names ending in '-wich' pay tribute to their origins in close proximity to ancient brine springs (Kurlansky 2003).

Alchemists still ascribed magical properties to salts: *The essential Saltes of Animals may be so prepared and preserved, that an ingenious Man may [...] raise the fine Shape of an Animal out of its Ashes at his Pleasure; and by the lyke Method [...] call up the Shape of any dead Ancestour from the Dust* (Mather 1702). Apart from spooky, cabbalistic visions and the magical character of the early concept of essential salts, interestingly enough, they did realize the essential nature of salt to humans, as did the ancient king when he embraced his lost child and made her queen of his lands.

In this regard, physiologists have followed in their footsteps. Today, research focuses mainly on the central and peripheral regulation of salt intake, balance and excretion.

Central homeostatic nuclei are responsible for the regulation of an appropriate salt intake/appetite (McKinley *et al.* 2015), with manifold interfaces to other regulatory centres (Carmichael *et al.* 2015). With the increase in availability of meat and meat products, the coin has turned. Dietary intake of sodium far surpasses the physical need, but salted food is still perceived as tasty. This 'salt gluttony' may, for example, be learned, or, on the other hand, evolutionary (reviewed in Zakrisson, 2015).

The ancient king, mind, was unable to swallow the unsalted food. However, what would have happened, had he oversalted? Among the five basic tastes sweet, sour, bitter, (sodium) salty and umami, 'salty' is unique: while bitter and sour stimuli are innately aversive, sweet and umami are appetitive, but increasing salt concentrations convert an appetitive stimulus into an aversive one and thus prevent harmful health effects of high levels of dietary salt. Recently, Oka *et al.* (2013) have shown how the body accomplishes this astonishing reaction: high sodium concentrations in the food apparently recruit the primary aversive taste pathways by activating the sour- and bitter-taste-sensing cells. Sodium channels, with, among others, their role in transmitting the appetitive effect of low concentrations of dietary sodium chloride (Oka *et al.* 2013), are a classic playground for physiologists of all specializations, given their role in, for example, excitable cells (Salvage *et al.* 2015) (Jeevaratnam *et al.* 2015).

Feedback systems such as the renin–angiotensin–aldosterone system (RAAS), renal nerve activity (DiBona & Kopp 1997) (Khan *et al.* 2014, 2015) (Barry & Johns 2015), peptide regulators (atrial and brain natriuretic peptide) and cardiovascular variables (Hall *et al.* 1990) regulate sodium balance (reviewed in: Isaksson *et al.* 2014). Therein, the kidneys play a major role, embedded in an intricate and interwoven network of electrolyte and blood pressure regulation mechanisms (Healy *et al.* 2014) (Damkjaer *et al.* 2014).

Purinergic signalling mechanisms (Franco *et al.* 2015) (Mironova *et al.* 2015) (Menzies *et al.* 2015) are one hot topic, with adenosine signalling as a promising target for drug development (Chen *et al.*

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2013) (Sällström *et al.* 2014) (Kim *et al.* 2015) (Welch 2015).

Although the jury is still out on the exact benefits of dietary restriction of sodium intake for cardiovascular patients, recent results link sodium intake to disturbances in vasoactive substance balance (Heimlich *et al.* 2015) (Palm 2015) and other pathologies, such as autoimmune disease (Kleinewietfeld *et al.* 2013) (Wu *et al.* 2013), even though very preliminarily so (O'Shea & Jones 2013).

However, given all we know about salt and our bodies, it seems that we have not yet in full overcome the magical thinking of the ancient alchemists: to this end, have a look at the elaborate theories, marketing strategies and revenues generated by the followers of Wilhelm Heinrich Schuessler and the effects they ascribe to low-dose mineral compounds (Saul 2015) (DHU 2015). The promise of a cure without side effects seems too irresistible, even to modern, maybe even science-literate, contemporaries.

Conflict of interest

None.

Pontus B. Persson
Institute of Vegetative Physiology, Charité-Universitaetsmedizin Berlin, Berlin, Germany
pontus.persson@charite.de

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