Bioactive nutrients in animal-sourced foods: cases for creatine, carnitine and taurine

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INTRODUCTION

Animal-sourced foods are rich sources of nutrients including protein, fat, vitamins, and minerals. The protein portion is made of essential and non-essential amino acids. Animal-sourced foods are also a source of amino acid derivatives with unique biological activities. The presence of many of these amino acid derivatives (i.e. bioactives) have been known for years, but our understanding of these continues to evolve. Bioactives are not considered essential (i.e. they can be made by the human body), but their increased consumption can be valuable for health under certain conditions (Seline & Johein, 2007; Wu, 2020). Emerging evidence suggests that a lack of these bioactives in the diet (e.g. vegetarian diets) could negatively impact development of children and increase the risk of some chronic diseases. The present review will explore three bioactives, specifically creatine, carnitine and taurine, examining the synthesis of these, their accepted functions/emerging roles, levels in animal-sourced foods compared to other foods, and to what extent amounts present in animal sources can contribute to human health promotion.

SUMMARY OF KEY FINDINGS

- **Although creatine, carnitine and taurine can be synthesized by the human body (hence not considered essential), dietary sources might be more important than previously thought.**
- **Adequate supplies of these bioactives are crucial during pregnancy and infancy.**
- **These bioactives may provide long-term health benefits when consumed in the diet, such as improved brain health, and deficiencies of these compounds are observed in some patients with chronic health conditions.**
- **Animal-sourced foods are the only sources of creatine and the primary sources of carnitine and taurine in the diet. Seafood and meats contain more of these bioactives than dairy and eggs.**
- **Animal-sourced foods provide value in the diet beyond the provision of traditional nutrients like protein and iron.**

CREATINE

Synthesis and functions

Creatine is synthesized from the amino acids arginine, glycine and methionine, mainly in the kidney and liver, circulates in blood and is taken up by muscle. Muscle contains about 95% of the body's creatine, and most is found as creatine phosphate (CP). The energy for muscle contraction is provided by phosphate cleavage from adenosine triphosphate (ATP). There is, however, a limited amount of ATP in muscle, and to overcome this, ATP is resynthesized rapidly by phosphate donation from CP (Balestrino & Adriano, 2019; Wyss & Kaddurah-Daouk, 2000). A major function of CP is, therefore, to act as an energy buffer providing high energy phosphate to help maintain ATP concentrations.

Requirements

It is estimated that young adults breakdown and need to replenish about 2 g of creatine per day and this amount decreases with age (Cockcroft & Gault, 1976). Adults can make about 1 g of creatine per day and omnivores get the remainder mainly from dietary sources.. Needs for creatine are not static and greater amounts are needed during intensive exercise, pregnancy, lactation, tissue injury, ischemia, diabetes and chronic kidney disease (Post et al., 2019; Wu, 2020). Since creatine is found exclusively in animal-sourced foods, vegetarians can face challenges meeting extra demands and have been found to have lower contents of serum (Delanghe et al., 1989) and muscle (Lukaszuk et al., 2002) (Brosnan & Brosnan, 2007) creatine. Creatine synthesis also requires vitamin B_{12} which poses further risks for vegetarians, as they often require vitamin B_{12} supplementation (Pawlak et al., 2013).

Dietary Sources

Creatine is found exclusively in foods of animal origin (Balestrino & Adriano, 2019; Hou et al., 2019). Fish and meat are the richest sources of dietary creatine, but dairy and eggs also contain some (Table 1). Some studies have been performed to examine the effects of diet on creatine content in beef. No differences in creatine levels were found between beef reared under organic compared to conventional conditions (Ribas-Agustí et al., 2019) or when feeding concentrate compared to a grass silage diet (Koutsidis et al., 2008). Supplementing the diet with 10% whole linseed, however, increased the creatine concentration of ribeye steaks by 0.4 mg/g (Marino et al., 2019). Cuts containing more white muscle fibers, such as the loin, also have more creatine that cuts with more red muscle fibres, such as the clod heart (Purchas & Busboom, 2005). So far, no studies have been performed to look at possible effects of cattle breed on creatine content.

Table 1. Creatine content in various foods

Food	Creatine content (mg/100 g serving)
Herring[1]	650-1000
Pork[1]	500
Beef[1]	450
Chicken[1]	380-430
Tuna[1]	400
Cod[1]	300
Milk[1]	10
Egg[2]	5.2

Values obtained from [1]Balestrino and Adriano (2019) and [2]Pimenta et al. (2023)

Emerging Roles

Cars can run on regular fuel, but adding more octane enhances performance. Similarly, people can survive without creatine in the diet but creatine consumption can be beneficial for muscle growth, as well as brain and metabolic health. Omnivorous diets provide 0.75-1.5 g of creatine per day, but it has been estimated that consumption of 2-4 g per day is optimal to promote general health (Kreider & Stout, 2021). Creatine provides a rapid source of energy for skeletal muscle contraction, but the need for rapidly regenerating ATP (i.e. supplying energy) can be critical in many other cells and tissues, including brain cells and heart tissue. As a consequence, the dietary supply of creatine has potential to impact many aspects of growth and metabolism, and as consequence overall health.

Dietary creatine enhances muscle growth which is important to help children achieve their growth potential (Korovljev et al., 2021). Creatine supplementation has been shown to enhance lean mass in athletes (Farshidfar et al., 2017) and help to prevent loss of muscle (sarcopenia) in the elderly (Brose et al., 2003; Dolan et al., 2019; Wu, 2020). A rapid supply of energy from CP is also important for the proper function of many nerves, and as might be expected, can affect many aspects of brain function including cognition, memory and/or executive function (Kreider & Stout, 2021), which are often impacted as part of the aging process. Creatine supplementation has been found to improve reaction time and mood in sleep-deprived individuals (McMorris et al., 2006), and may be beneficial for patients with some types of depression, including major depressive disorder (Kious et al., 2017; Yoon et al., 2016) and bipolar disorder (Toniolo et al., 2018). In one particular study, prevalence of depression was also found to be 42% lower among adults consuming 0.70-3.16 g of dietary creatine daily compared to less than 0.27 g of dietary creatine daily (Bakian et al., 2020).

Creatine supplementation also appears to help type 2 diabetes patients by promoting glucose uptake by muscles (Alves et al., 2012; Gualano et al., 2011). In addition, creatine may have a role in controlling post-workout inflammation (Bassit et al., 2008; Deminice et al., 2013) and inflammatory bowel disease (Glover et al., 2013; Wallimann et al., 2021). Further, creatine supplementation in mouse cancer models suppresses tumour growth, likely by meeting the energy demands of immune cells (Di Biase et al., 2019).

Potential usefulness of creatine from animal-sourced foods

Creatine consumption can have many beneficial health effects, and the question is to what extent animal-sourced foods, including beef, can contribute to this. On one hand, under normal circumstances our bodies can produce the creatine we require for normal functioning and as such it is not considered an essential nutrient. Others suggest that additional creatine (beyond the amounts in a regular diet) could actually be beneficial and supplementation should be encouraged (Balestrino & Adriano, 2019). On the other hand, recent research is suggesting that dietary creatine does seem to positively impact health and wellness (e.g. promoting muscle growth in children) and not consuming it has negative impacts (e.g. depression). Further, many of the conditions that have been found to benefit from creatine supplementation are on a continuum and not absolute in nature. For example, the elderly don't lose all their muscle mass or become forgetful overnight. The benefits of incremental increases in creatine consumption, and the downsides of not consuming it, thus need to considered/studied where longer term advantages may be offered.

CARNITINE

Synthesis and functions

Carnitine is made from the essential amino acids methionine and lysine (Borum, 2014), and its main function is transporting fatty acids into cell mitochondria (Reda et al., 2003). Fatty acids are broken down (oxidized) in the mitochondria to provide energy, and to get them into the mitochondria, fatty acids are bound to carnitine and this complex is transported into the mitochondria by a transporter, Carnitine acyltransferase I (Borum, 2014).

Requirements

For the general population, there is no official recommended intake of carnitine, but humans excrete approximately 0.8mg/kg of carnitine daily, thus a 70 kg male needs to either synthesize or consume approximately 60 mg of carnitine daily to replenish the body's carnitine stores (Demarquoy et al., 2012). L-carnitine is considered essential for newborns since they have a limited capacity for synthesizing carnitine (Shenai & Borum, 1984). Carnitine levels are also markedly reduced over the course of pregnancy (Cederblad et al., 1986). Omnivorous diets provide about 80% of the carnitine in the body and the remainder is synthesized (Rigault et al., 2008). It is unclear whether vegetarians have adequate levels of carnitine since some researchers have found no differences in plasma carnitine levels between vegetarians and omnivores (Cha et al., 2002), whereas others have found reduced plasma carnitine in vegetarians, especially in children (Lombard et al., 1989). As iron is a cofactor for carnitine synthesis, people with iron deficiency (e.g. some pregnant women and vegetarians) may not be able to synthesize enough carnitine (Keller et al., 2009).

Carnitine levels in foods

Meat, particularly red meat, has a higher content of carnitine than fish, dairy, eggs and fruit/vegetables. Concentrations of carnitine in various foods are summarized in Table 2.

Table 2. Carnitine content in various foods

Food	Carnitine content (mg/100 g serving)
Goat meat[1]	183
Venison[1]	74
Beef[1-3]	56-74
Pork[1]	18
Chicken[1]	16
Avocado[4]	8.1
Salmon[2]	6
Pea[4]	5.7
Milk (1.5%)[3]	3.5
Cod[4]	1.8
Egg yolk[4]	0.8
Carrot[3]	0.4
Egg white[4]	0.3

Values were obtained from [1]Shimada et al. (2004), [2]Rigault et al. (2008), [3]Seline and Johein (2007), [4]Demarquoy et al. (2004).

Emerging Roles

Although humans can synthesize carnitine, recent evidence suggests that carnitine deficiency can sometimes occur leading to negative health effects. For example, frail elderly individuals (over 65 years) have lower carnitine levels than their peers (Malaguarnera et al., 2020). Some individuals with diseases including cancer (Cruciani et al., 2004), heart failure (Kristian & Lestari, 2020), diabetes (Shaukat et al., 2021), and Huntington's disease (Cuturic et al., 2013) also have carnitine deficiencies. Carnitine supplementation has been found to benefit people suffering from different types of cancer (Cruciani et al., 2004), heart failure (Kristian & Lestari, 2020), diabetes (Wang et al., 2021) and alcohol use disorder (Bota et al., 2021). There is also potential for using carnitine supplementation for weight management, particularly overweight and obese individuals (Askarpour et al., 2020).

Supplementation with L-carnitine has also been found to reduce inflammation in humans, particularly when taken for more than 12 weeks (Haghighatdoost et al., 2019), and could have beneficial effects in patients with sepsis (Keshani et al., 2022) and cardiovascular disease (Nachvak et al., 2023; Sahebkar, 2015). Carnitine supplementation may also increase cognitive function in the elderly (Malaguarnera et al., 2007) and children with autism spectrum disorders (Geier et al., 2011). Carnitine supplementation may be helpful for the treatment of migraines in individuals with carnitine deficiency (Charleston et al., 2021).

Potential usefulness of dietary carnitine

Carnitine consumption can have many health benefits, and it is important to determine to what extent beef and other animal-sourced foods can contribute to this. Carnitine in the diet can be absorbed more efficiently than carnitine from supplements (Evans & Fornasini, 2003), and given that diseases associated with carnitine deficiency develop over time, it is conceivable that dietary consumption of carnitine may be advantageous over the long term.

TAURINE

Synthesis and functions

Taurine is made from the sulfur-containing amino acids cysteine and methionine, and up until recent decades, its main role was considered to be in fat digestion. Specifically, taurine is bound to cholic acid to form taurocholic acid, which is secreted in bile to emulsify fat and aid in its digestion (Marcinkiewicz & Kontny, 2014; Wu, 2020). Taurine is one of the most abundant free amino acids in the body, and as such, it is thought to be important to help maintain osmolarity (i.e. water balance) of cells (Schaffer et al., 2009).

Requirements

Currently, requirements for taurine have not been established because the human body can synthesize taurine in adequate amounts under most circumstances. Adults synthesize from 50-125 mg of taurine per day, but this depends on adequate intake of its precursor sulfur-containing amino acids (Wu, 2020). Taurine is, however, essential for fetuses and newborns (Tochitani, 2022). People who do not consume animal-source foods could be at risk of taurine deficiency because cysteine and methionine concentrations are low in many plant-sourced foods and taurine is absent in most plant-sourced foods (Wu, 2020). Indeed, Laidlaw et al. (1988) found that plasma taurine levels of healthy vegans were reduced compared to omnivores. In contrast, Rana and Sanders (1986) found no differences in plasma taurine levels in vegans compared to omnivores. Breast milk from vegetarian compared to omnivore mothers, however, has a lower taurine concentration (Rana & Sanders, 1986). This is important given that dietary taurine is necessary for optimal neural development (Wharton et al., 2004) and that taurine deficiency may lead to retinal dysfunction in children (Geggel et al., 1985). Taurine synthesis can also be reduced under disease conditions such as diabetes, cancer, and sepsis (Marcinkiewicz & Kontny, 2014; Wu, 2020).

Taurine levels in foods

Most fruits, vegetables, nuts and grains are devoid of taurine (Laidlaw et al., 1990). Shellfish and the dark meat of poultry are major sources of taurine, but beef, pork and fish also have relatively high taurine levels. Taurine content in various foods are summarized in Table 3. Beef cuts with more red muscle fibers such as clod heart and flat iron steaks have more taurine than cuts with more white muscle fibers such as loin (Purchas & Busboom, 2005; Purchas & Zou, 2008). Meat from pasture-finished cattle has more taurine than meat from grain-finished cattle (Purchas & Busboom, 2005), and cattle breed can also effect taurine levels in meat (Purchas & Zou, 2008).

Table 3. Taurine content in various foods

Food	Carnitine content (mg/100 g serving)
Scallops[1]	827
Mussel[1]	655
Clam[1]	520
Turkey- dark meat[1]	306
Chicken- dark meat[1]	169
Cod[2]	108
Beef- clod heart[4]	103
Beef- flat iron[5]	60
Salmon[2]	108
Pork[1-2]	40-61
Beef- loin[4-5]	30-43
Turkey- white meat[1]	30
Chicken- white meat[1]	18
Seaweed (Hirakusa)[6]	12.5
Plain yogurt[1]	3.3
Milk (2%)[1]	2.3
Egg yolk[6]	0.75
Egg white[6]	0.10
Beans[6]	0.7
Hazelnut[6]	0.6
Cashew[6]	0.5
Bread[1]	Not detectable
Lettuce[1]	Not detectable

Values obtained from [1]Laidlaw et al. (1990), [2]Gormley et al. (2007) [3]Jensen et al. (2014), [4]Purchas and Busboom (2005), [5]Purchas and Zou (2008) [6]Larsen et al. (2013) and [7]Cataldi et al. (2004).

Emerging roles

Recently, taurine has been found to have functions beyond its role in fat digestion, including anti-inflammation and neuromodulation (Schaffer & Kim, 2018). Hence taurine consumption could potentially provide many health benefits. During immune activation, taurine can be metabolized to compounds that are powerful bactericides, and powerful anti-inflammatory signalling molecules, and there is evidence that taurine may be efficacious across multiple diseases where inflammation is involved (Marcinkiewicz & Kontny, 2014). The importance of taurine is highlighted in those suffering from chronic sinusitis (inflammation of the nasal passages), where people with sinusitis had a 50% reduction in blood taurine while no other amino acids were affected (Atila & Atila, 2022), and taurine may have therapeutic value in treatment of allergic disorders (Zhou et al., 2020). Further, taurine supplementation reduced inflammation in burn victims (Lak et al., 2015).

Additionally, recent studies suggest that taurine is important for brain health. For example, elderly individuals with a history of consuming taurine-rich foods (i.e. shellfish and anchovy) had better cognitive function than those consuming less dietary taurine (Bae et al., 2017). Further, taurine levels were reduced in the serum of Parkinson's disease patients and this was associated with increased severity of motor symptoms (Zhang et al., 2016). There was also a reduced risk of stroke among non-smoking women that had higher compared to lower serum taurine levels (Wu et al., 2016). Taurine supplementation also reduced inflammation and improved clinical outcomes in patients with traumatic brain injury (Vahdat et al., 2021).

Dietary taurine was associated with lower metabolic syndrome risk in adolescent girls by improving serum lipid profiles (Ishikawa et al., 2010) and reduced the risk of developing cardiovascular disease (Yamori et al., 2010) among middle-aged men and women. Further, increasing dietary taurine from approximately 22 mg per day to 40 mg per day over the course of one year reduced the risk of type 2 diabetes among prediabetics over 65 years of age (Díaz-Rizzolo et al., 2021). Taurine supplementation may be an effective supporting therapy for the management of congestive heart failure (Azuma et al., 1992), may lower blood pressure (Sun et al., 2016), and has potential for the treatment of other cardiovascular diseases and muscle diseases (Schaffer & Kim, 2018). In addition, taurine appears effective in the treatment of mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS), and offers a new approach for the treatment of metabolic diseases such as diabetes (Schaffer & Kim, 2018).

Potential usefulness of taurine from animal-sourced foods

Overall animal food sources can supply taurine for health promotion. In beef, the cuts, breeds and feeding systems influence taurine levels.

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