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Invited Commentary

Nutrition is medicine: dietary inhibition of hepcidin expression

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Poor Fe status, often characterised as Fe deficiency (ID, poor Fe stores) and Fe-deficiency anaemia (IDA, ID with diminished Hb), affects billions of people in both the developing and developed world[1,2]. Poor Fe status affects both physical and neuropsychological performance, and has profound effects on work performance and productivity[3]. Historically, efforts to treat and prevent ID and IDA have included the provision of added Fe to the diet in the form of fortification and supplementation, and recent systematic reviews have indicated that these countermeasures appear to be somewhat effective in restoring Fe status[4,5]. However, the discovery of hepcidin, often described as the central regulator of Fe homeostasis, may provide a new target for the treatment and prevention of ID and IDA. Hepcidin regulates Fe status primarily through its effects on Fe export from the enterocyte, macrophage and hepatocyte, where it binds and degrades ferroportin 1, the export protein responsible for cellular Fe egress[6].

Due to the central role of hepcidin as a mediator of Fe homeostasis, recent human studies have explored the use of a series of pharmacological agents, such as heparin[7] and IL-6 antagonists[8] as inhibitors of hepcidin expression. However, significant questions remain regarding the efficacy and safety of these compounds for the maintenance of Fe status in humans. In this edition of the *British Journal of Nutrition*, Mu *et al.*[9] detail a novel set of studies investigating the role of extracts from foods, such as black soyabean, black fungus, black sesame seeds and persimmons for the inhibition of hepcidin expression in cells and for the maintenance of Fe status in animals.

In these studies, Mu *et al.*[9] first screened extracts of the foods for their effects on hepcidin gene (hepcidin antimicrobial peptide; HAMP) expression in human hepatocytes (HepG2 cells). After discovering that extracts from one of the foods, black soyabean seed coat extract (BSSCE), affected hepcidin expression in the cell model in a dose- and time-dependent manner, mechanistic studies determined that BSSCE significantly reduced the phosphorylation of transcription factors responsible for activation of the HAMP gene. Similarly, BSSCE inhibited the effects of factors known to stimulate HAMP expression, including bone morphogenic protein 6 and IL-6. Importantly, BSSCE did not affect cell viability.

Subsequently, the investigators studied the effects of BSSCE on hepcidin expression and Fe homeostasis in mice. In these studies, mice (C57BL/6) were provided standard rodent diets containing 2% BSSCE for up to 30 d. Hepatic hepcidin expression was reduced by over 50% as soon as 1 d following initiation of the experimental diet. Splenic Fe was reduced by day 15, and significant increases in serum Fe levels were observed by day 7. Similarly, erythrocyte counts, Hb concentrations and haematocrit levels were elevated in the BSSCE-treated animals over the course of the study.

The experiments detailed in the Mu *et al.*[9] study may represent a novel dietary approach to the treatment of ID and IDA through the inhibition of hepcidin expression. Clearly, subsequent studies will be required to assess the safety, efficacy and practicality of treating humans with poor Fe status with foods such as black soyabean, although the use of nutrition as medicine may hold great promise for the future, especially in the developing world where access to foods with highly bioavailable Fe or advanced medical resources, such as pharmacological agents, may be limiting.

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British Journal of Nutrition

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