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Relationship between the Chromium or Chromium Compounds on Immune Functions in Animals

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Abstract

There is a close relationship between the trace elements and the health of animal, especially the immune function, which is greatly, influenced by some trace elements, such as chromium, an essential element in animals. The effects of chromium on the immunity have been confirmed, thus, the aims of this review are to clarify the relationship between the chromium or chromium compounds on immune function in animals from the aspects of the development and growth, histological structure of the immune organs, non-specific immunity, humoral immunity, cellular immunity and cytokines.

Keywords: Chromium; Non-specific immunity; Humoral immunity; Cellular immunity; Cytokines

Introduction

Chromium (Cr) is firstly discovered by a French chemist-Louis Vauquelin in 1797 in the natural environment as an transitional metallic elements, which exists in a number of different valence states, such as 0, 2, 3 or 6 valence, but 3 valence (Cr^{3+}) is the most stable form existing in animals. However, for a long time, chromium is considered to be a toxic and harmful substance to animals. Till to 1957, Mettz and Schwarz found that the main active component of the glucose tolerance factor in beer yeast was trivalent chromium ion (Cr^{3+}). In the following research, it has been found that there were many biological functions of chromium, such as promote the action of insulin for the utilization of sugars, proteins and fats, and enhance the immunity of animals and so on.

The effects of chromium on the animal immunity has been proven, which can improve body's immunity and enhance the ability of disease resistance, thus reduce the susceptibility of animals to disease. However, at present, the relationship between the chromium and immune functions is not quite clear. Therefore, this review gives an overview of the relationship between chromium and the immune functions in animals from the aspects of biological functions of the essential trace element-chromium, the effects on the growth and development of immune organs, nonspecific immunity, humoral immunity, cellular immunity and cytokines, we hope this review will provide a helpful foundation on the relationship between chromium and immune function in the future studies. Due to constraint of space only a limited number of studies have been cited.

Biological Functions of Chromium

Ionic chromium has no biological activity, but the organic or inorganic form chromium compounds are more easily absorbed and have higher biological utilization rate in animals [1].

As an essential trace element, chromium is required for normal carbohydrate metabolism by regulating insulin action [2]. It also involves in the mechanism of sugars, proteins, fats and nuclear acid [3,4]. If the chromium deficiency, the utilization of the above mentioned substance would be inhibited [5-8]. In addition, chromium can promote the growth performance of animals [9-12], and promote some enzymes activities, and is beneficial to maintain the integrity and stability of the nucleic acid, helpful to the glycine, serine, methionine and other amino acids to be stored or uptake in the tissues [13,14]. Chromium also has beneficial effect on both muscle strength and body composition [15]. Chromium deficiency in diet may result in slow growth, impaired glucose tolerance, diabetes and coronary artery diseases [16].

The effects of chromium on the development and growth of immune organs

Immune organs mainly consist of lymph nodes, thymus, spleen and bursa of Fabricius (unique to poultry). As the important immune organs in animals, whose weight has closed relationship with the immune functions [17]. Therefore, to a certain extent, the immune organ index (the ratio of immune to body weight) can reflects the immune function of the animal. It has been reported that chromium can increase the absolute weight of the thymus, spleen and bursa of Fabricius in broiler [18], for example, the inorganic chromium ($CrCl_3$) could improve the thymus, spleen and bursa of Fabricius index [19,20]. In addition, the organic chromium also has some effects of the immune organs, the collagen peptide-chromium (β) chelate can inhibit the decrease of the growth of the immune organs and immune organ index induced by mesoxyalyurea [21].

The effects of chromium on the histological changes

Few studies about the chromium on the histological changes. The chromium can inhibit the pathological changes which induced by heat stress (for example, volume of lymphatic nodules amplified, lymph beside artery of white pulp were more thicken and the number of ellipsoid increase) [22].

The effects of chromium on the nonspecific immunity

Nonspecific immunity is a inherent immune, which can response to all kinds of invasion of pathogenic microorganisms invasion rapidly,

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and also plays an important role in the beginning period of specific immune process. Some studies reported that additional chromium (β) increase the level of lysozyme in rat [23,24]. The chromium (VI) can decrease the number and the phagocytosis of phagocytes, neutrophils, macrophage, and inhibit the activity of lysozyme in *Cyprinus carpio* [25], but some other studies reported that $CrCl_3$ and chromium picolinate (CrP) have no significantly effects on the lymphocyte and neutrophils [26], and the additional chromium has no effects on the nonspecific immunity of the *Eriocheir sinensis* [27]. It can be seen that the influence of chromium on the non-specific immunity is still controversial and needs to be further studied.

The effects of chromium on the humoral immunity

The humoral immunity is reflected by the production of antibodies by B cells, therefore, the B cells are the major cells which responsible for humoral immunity. Animals studies have been proven that the chromium has significantly effects on the humoral immunity. $CrCl_3$ and CrP can enhance the production of antibody and improve the humoral immunity of pig or rabbits [26,28], chromium propionate supplementation can increase the serum antibody titer and immunoglobulin content in weaned pigs [29], chromium pyridine carboxylate or lysine chromium can increase the globulin level of the cows in lactation period [30]. In addition, supplementation of the trivalent chromium (CrP and chromium pyridine carboxylate) could significantly increase the content of immunoglobulins under the condition of severe stress [31,32]. Chromium can also significantly enhance the antibody titer of T lymphocytes to bovine serum albumin (BSA) [33], and to the *Pseudo rabies virus* (PRV) in weaning piglets [33,34]. Dietary chromium supplementation can increase the antibody titer to the serum newcastle disease [36,32], and enhance the humoral immunity of broilers [37,38].

The effects of chromium on the cellular immunity

T cells is the mainly cells participate in the cellular immunity. A lot of studies have been confirmed that the supplementation of the chromium has positive effect on the cellular immunity. Chromium could increase the conversion of peripheral blood lymphocytes by interactivity with insulin and cortisol [39]. Chromium can improve the proliferation of the T lymphocytes [40], and enhance the cellular immunity [38]. Organic chromium can increase the cytolytica ctivity of T and NK cells by activating these immune cells [21]. Dietary $CrCl_3$ significantly improve the conversion rate of total blood lymphocyte in rabbits [28], increase the conversion rate of lymphocyte in piglet (Van Heugten and Spears, 1997). CrP can also increase the lymphocyte conversion rate treated with phytohemagglutinin (PHA) [34,35] or heat stress [22], enhance the conversion rate of T lymphocytes in peripheral blood and spleen [23].

The effects of chromium on the cytokines

Cytokines are the small molecule proteins with biological activities which synthesized and secreted by immune cells (such as macrophages, T cells, B cells, NK cells, etc.) and some non- immune cells (endothelial cells, skin cells, fibroblast, etc.). As mentioned above, the chromium or chromium compounds pose effect on immune organs or immune cells, so it will affect the cytokines directly or indirectly. CrP can increase the level of serum interleukin-2 (IL-2) and interleukin-6 (IL-6) in pigs [41]. In addition, in vitro experimental study indicated that chromium could increase the level of interleukin-4 (IL-4), interferon-γ (IFN-γ) in monocytes [39], and the level of tumor necrosis factor (TNF-α) in macrophage [42] or monocytes [43]. Other studies also reported that chromium affect the secretion of IL-12, and the mRNA expression of TNF-α, IL-1α, IL-6, INF-α, macrophage colony stimulating factor (M-CSF), transforming growth factor (TGF-β) [44].

The Mechanisms of Chromium on Immunity

Chromium, as necessary trace element, whose effect on the immune regulation has been confirmed. The mechanisms of action of chromium on immunity are related with the effects of chromium on the insulin and cortisol [45-47]. Some other studies have also proved that after the immune system is activated by chromium, the proliferation rate and the number of T and B lymphocytes significantly increased [44]. Furthermore, chromium can improve the immune function by regulating the activity of some immune related enzymes and content of immunoglobulin [48,49]. Chromium may also improve the immune function by enhancing the immune effect of the vaccine or by lowering cortisol level or other immune intermediates [50,35,34].

In addition, chromium can affect the biosynthesis of proteins [51,52] and RNA [53,54] in the nucleus, and it also participate in the maintain of DNA integrity [55] and this may be the molecular mechanisms of the chromium on immunity.

Prospective Research of the Chromium

With the continuous development of molecular biology and genetic engineering technology, a large number of new and effective chromium functional food or feed additives will be synthesized, and will be used to cure some metabolic disease of humans and animals. The relationship between the chromium and the cancer or other diseases remains to be elucidated, and the histological changes of the tissues induced by chromium should be clarified. In the poultry production, the mechanism of action, biological titer of different forms, and the supplementation dosage in the diet in different physiological period needs to be further studied in the future.

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