

Review

Camel immunobiology: implications on mastitis-resistance and future therapeutics

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Abstract

Each living organism from microbes to primates, has its own immune regime, which differs in its strategies but most of the species are susceptible to infection by pathogens. Nevertheless, camels are resistant to most infections, especially mastitis as well as they can endure the stress in contrast to the cattle, therefore this study has focused on the immune perspective and occurrence of mastitis in the both species as it is very rare in camels. Also, summarized a new insight of utilizing the camel's milk for the human health and reducing possible zoonotic pathogens. A noticeable difference in the immunity of both species and new trend of therapy have been demonstrated. Further research must be conducted to identify the therapeutic effect of camel's milk on the human.

Keywords: camel, cattle, immunity, mastitis.

المناعة البيولوجية للإبل: وما تعكسه من مقاومه الإصابة بالتهاب الضرع واستراتيجية العلاج المستقبلي

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الكلمات المفتاحية: الإبل، الأبقار، المناعة، التهاب الضرع

الخلاصة

إن لجميع الكائنات الحية (من الميكروبات إلى الكائنات العليا) أنظمة مناعية مختلفة بحسب الآلية الفسيولوجية لأدائها إلا أن أغلب تلك الكائنات معرضة للإصابة بالجراثيم، لكن الإبل على وجه الخصوص تمتلك مقاومة لأغلب تلك الأمراض وخصوصاً مرض التهاب الضرع. كما يمكنها أن تتحمل ظروف الإجهاد خلافاً للأبقار لذلك ركزت المقالة الحالية على الجانب المناعي وحدث التهاب الضرع في الأبقار والإبل كون المرض نادر الحدوث في الأخير. كما لخصت التوجهات الحديثة لاستخدام حليب النوق كمنتج صحي للإنسان ومقللاً للعديد من الأمراض المشتركة. تم ذلك من خلال استعراض المراجع البحثية المتضمنة الجوانب المناعية في كلا النوعين والتوجهات العلاجية الجديدة مع التوصيات اللازمة بإجراء المزيد من الدراسات في هذا المجال.

Introduction

Camel's domestication has increased in several Arabic countries not because they can produce meat and milk, but also, they can endure the harsh conditions and resist infection (1). A considerable amount of research has been carried out to explain the resistance of camels to various causative agents, in comparison to cattle. However, there is no research that has summarized the main immunological features of the camels. Consequently, this research has focused on the strategies that permit camels to resist mastitis as an important disease which affects the welfare system and predicts new scientific insight for getting the cure of some illnesses and a precursor of some healthy products.

In spite of the extreme environmental conditions in the deserts such as: harsh sun rays, high or low temperature habitats, sand storms, starvation and drought, indeed, these are considered as stressful causes to the immune system. In addition to endure these conditions; camels produce milk and meat due to its unique physiology and resistance to pathogens (2). In contrast, cattle are sensitive to numerous diseases, including mastitis (inflammation of the mammary gland and contamination of milk). This essay will focus on the immunity in camels, especially against mastitis. In addition, it will illustrate how the camels can resist the infection in comparison with cattle. Finally, it will reveal what the new insight of using camel's milk as an alternative medicine.

Development of research into camel and cattle immunity against mastitis

Immunity in general refers to the resistance of the body or the response of a specific and sensitive immune cell against pathogens. This could be achieved in two pathways: firstly, known as the innate immunity, which means the presence of various physiological features such as: host specification, age, pace of immune response, and host gene expression (3).

Secondly, the acquired immunity, which arises due to specific response against the causative agent. This kind of immunity will respond rapidly if the body is invaded by the same antigen consequently. Camels in particular, have a high level of innate mechanisms against infectious diseases (4). Basically, the immune system of the camels and cattle has a mutual activity. In the innate immunity that helps the both animal species to resist harsh conditions but in camel's body temperature; it is characterized by its daily fluctuation, meaning they can endure the elevated heat (1,2) whereas there is no such a mechanism in the cattle immunity. The second one called acquired immunity, which plays an important role as a cellular immune pathway that have a crucial mechanism through the lymphatic system and production of immune active substances such as: reactive nitrogen intermediate, reactive oxygen intermediate, interferons, and tumour necrosis factor. The humoral immunity is also highly developed in camels, that is responsible for the production of specific antibodies (5). There are several immunological organs such as: spleen, tonsils, lymph nodes, and intestinal Peyer's patches, and bone marrow, which is involved in this kind of immunity (6–9).

Camel's Unique IgG antibodies

The unique immunoglobulins, which have been widely speculated about the structure of the camel's immunoglobulins, in particular IgG. It can be divided into three secondary types (IgG1, IgG2, IgG3). Many researchers have revealed the similarity of the structure of the first type with those in the cattle because it contains heavy and light chains, whereas the second and third ones are quite different, they contain one part of heavy chain; each one consists of two parts: the constant domain (CH2, CH3) and the single variable domain (VHH) or nanobody, that consists of heavy chain merely (Figure 1). This part can be separated from the whole antibody to be

free (4,10,11). These mini-antibodies possibly has a suppressive effect on the β -Lactamase which is produced by most of the antibiotic resistant bacteria, whereas there is no any effect of cattle's

immunoglobulins against these super pathogen (12,13). It has been shown that these nanobodies pursue several therapeutic and diagnostic uses against many zoonotic infections (6,10,14).

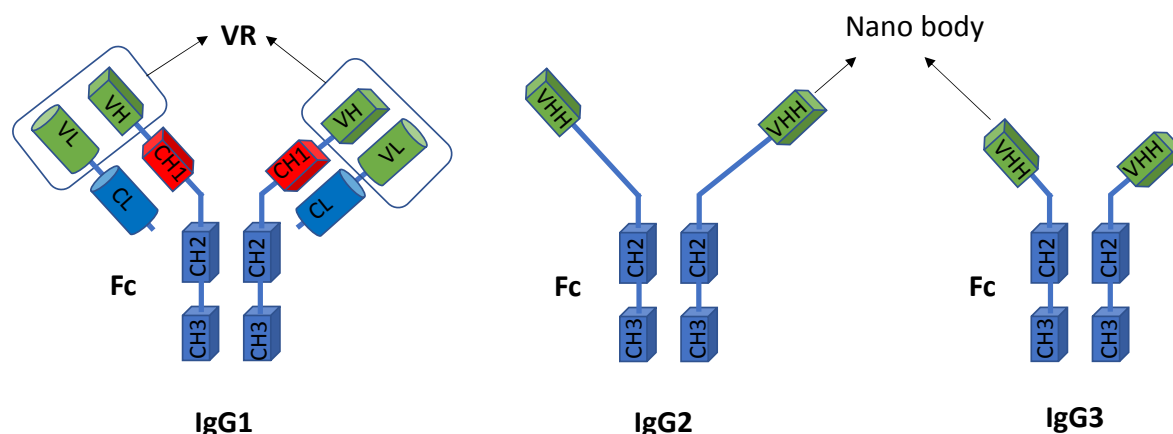


Figure 1. A diagram of Camelid's antibody

IgG1 is the conventional type of IgG, which has two heavy chains and two light chains. Each heavy chain has for domains three constant (CH1-3) and one variable (VH), while the light chains have two domains constant and variable (CL and VL) respectively. The variable region (VR) of both heavy chain and light chain consist the antigen recognition site. IgG2 and IG3 are the unique antibodies of Camelids (the Heavy Chain Antibody HCAb), which lacks the two light chains and CH1 domain of heavy chains. The antigen-recognition recognition site of these antibodies called Nanobody or single-domain antibody (sdAb) [adopted from (10)].

Potential therapeutic effect of the Camel's milk

Several studies revealed special and unique properties of the Camel milk that may put this camel product as an important industry as a natural adjuvant due to high content of free calcium ion, unsaturated fatty acid, anti-antioxidant (15–17). Another line of thought with the features of the camel milk, which is healthier than cattle because of the fact that it's content of a unique immunoglobulin as described

above. Therefore, we will illustrate the recent scientific research that demonstrates the future trend of using camel's immunoglobulins for the medical purpose. It can help in curing numerous diseases. For instance, employing of IgG in the treatment of snake venoms has reported by (10). while the treatment of hepatitis virus type C and certain hepatic tumors can be achieved by using camel's milk as a result of high content of milk's casein (17). The presence of unique insuline-like peptides in the Camel milk has encouraged to be used and successfully curing of type 1 diabetes via improving the glucose homeostasis (insulin secretion and receptor activity) (18) and cholesterol homeostasis that result as an anti-hypertensive effect (19,20). These effects could be linked to the presence of insulin-like proteins, lactoferrins, lactoperoxidase and lyzozymes, which also work as anti-bacterial agents against *Escherichia coli*, *Salmonella typhimurium*, *Staphylococcus aureus* and *Lactococcus lactis* as well as rotaviruses (21–27).

More experiments must be carried out to identify effects of using camel milk in the

manufacturing of chocolate on young people and its effects on prevention of modern life diseases such as obesity, diabetes, atherosclerosis, and cancer. On the other hand, climate changes, particularly, desertification has increased in the most Arab countries, this environment is unsuitable for cattle. Thus, new welfare systems must be applied in order to increase the quantity and quality of the camel milk and to manipulate the farmers to employ the camels instead of the cattle for this purpose.

Anticancer activity

It has been reported that camel milk can inhibit the *Cyp1A1* gene (a cancer-promoting gene), while it induces the expression of *NQO1* gene (a cancer inhibitory gene) in murine hepatoma cell line 1c1c7 (26). An anti-cancer protein in camel milk called alph-lactalbumin, that combines with oleic or linoleic acid which showed a cytotoxic effect on a human prostate cancer cell line DU145, furthermore, such combination showed remarkable stability at 60° C (28).

Immunobiological resistance to mastitis in she-camels

Several researchers have showed experimentally unique immunological characteristics that make camels have a significant resistance against myriad infections especially mastitis. To understand the role of camel's immune, this section aims to provide a discussion of the strategies by which they can resist mastitis in contrast to cattle.

Numerous bacterial, viral, parasitic, fungal, and nutrient deficiency diseases can cause serious symptoms to both species, but cattle are more sensitive than camels (29). The main pathogens that causes mastitis in she-camel are bacteria such as *S. aureus*, *Streptococcus spp*, *Streptococcus agalactia*, *Micrococcus spp*, *Corynebacterium pyogenes*, *E. coli* and *Pasteurella haemolytica* (29–32). Similarly, these causing mastitis in cows as well, with remarkable incidence due to *S. aureus*. The

prevalence of mastitis in camel has been estimated to occur in a percentage of about 25 % and the complications lead to 70 % drop in milk production, while the prevalence in cattle about 50 % (29). (33) identified another comparative feature in camels which is the bone marrow, as it has several functions such as producing the red and white blood cells including eosinophils. This cell type is considered as one of the most important immunological blood cells against parasitic infections and allergy reactions, it contains numerous granules in various sizes and shapes in comparison with those in cattle, which might mean it has a higher destructive effect against the pathogens. Another immune cell type is the mast cells, which is located in a high number all over the digestive system without any significant differences opposing to mast cell in cattle. However, this type of cell has an important physiological and immunological effect. This occurs through producing set of autacoids or vasoactive substances such as histamine and heparin (9).

Building on from the idea that mastitis has distributed in both species, it has an economic and public health value. Nevertheless, it is very rare in she-camels. Hence, the anatomical structure of the udder, teats, and gland cisterns are separated entirely with very narrow twin duct streak canals. Furthermore, the udder does not touch the earth, even when the animal in recumbent position, this act as an important mechanical prevention to infection (29). However, other researchers demonstrated that the milk contains inhibitors to pathogenic bacteria these includes: Lysozyme, immunoglobulins, lactoferrin and lactoperoxidase, these proteins involved with higher concentrations in comparison with cattle milk. All these inhibitors have an instrumental bactericidal effect; therefore, it is assumed that mastitis disease is uncommon in camels (17,24,34). Other studies have stated absence of *mecA* gene that is responsible for methicillin resistant

S. aureus and the rare of antibiotic resistance related genes in the *S. aureus* isolated from milk of Arabian she-camels (13,35). This possibly because of the presence of a small, soluble single-domain fragments derived from the unique variable region of dromedary heavy-chain antibodies which act as inhibitors to β -lactamase (12). It can be seen from the discussion above that camels are as well immunity as cattle, which in turn, it can produce healthy products for the humans. From the points raised in this review, the camels are able to survive, resist, and produce in stressful conditions due to an excellent corporation of the all immunophysiological mechanisms which owns. If the camels can produce very hygienic and curable milk with high resistance to infection through stressful conditions to other animals, potentially, they will perform better when they domesticated in a good environment. However, several studies have demonstrated a low production efficiency in camel compared with cattle in term of the meat and milk. Also, the reproductive behavior in camels is seasonal, whereas it persists all the year in cattle, but it can be predicted that the genetic engineering is going to combat these kind of problems as it has developed significantly, this absolutely will lead to ameliorate the camel's efficiency.

Another limitation concerned with the camel's welfare system which is inherently difficult therefore additional scientific courses are required for the farmers to increase awareness for Camels husbandry. It is predicted within a few years that a suitable welfare system will have been invented to obtain high quantitative and qualitative products, but this trend will not achieve if camel's welfare is not supported all over the world especially in the profitable habits. The phenomenon of the Camel's immunity needs to be considered and thorough research should be carried out in order to enhance them, especially to prevent the susceptibility against infection; the vaccination programs and better animal

husbandries the genetic engineering techniques will be the best strategies in this way.

Conflict of interest statement

None of the authors of this review has a conflict of interest that could bias this paper.

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