Biotechnology Advances 29 (2011) 860–868

Contents lists available at ScienceDirect

Biotechnology Advances

journal homepage: www.elsevier.com/locate/biotechadv

Research review paper

Application of chicken egg yolk immunoglobulins in the control of terrestrial and aquatic animal diseases: A review

Yongping Xu [a,b,c], Xiaoyu Li [a,b], Liji Jin [a,b,*], Yuhong Zhen [a,d], Yanan Lu [a], Shuying Li [e], Jiansong You [a], Linhui Wang [a]

[a] School of Life Science and Technology, Dalian University of Technology, Dalian 116024, China
[b] Ministry of Education Center for Food Safety of Animal Origin, Dalian 116620, China
[c] State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian 116012, China
[d] Department of Pharmacy, Dalian Medical University, Dalian 116044, China
[e] Dalian SEM Bio-Engineering Technology Co. Ltd., Dalian 116620, China

ARTICLE INFO

Article history:
Received 5 August 2010
Revised 29 June 2011
Accepted 11 July 2011
Available online 20 July 2011

Keywords:
Egg yolk immunoglobulin
IgY
Terrestrial
Aquatic
Disease control

ABSTRACT

Oral administration of chicken egg yolk immunoglobulin (IgY) has attracted considerable attention as a means of controlling infectious diseases of bacterial and viral origin. Oral administration of IgY possesses many advantages compared with mammalian IgG including cost-effectiveness, convenience and high yield. This review presents an overview of the potential to use IgY immunotherapy for the prevention and treatment of terrestrial and aquatic animal diseases and speculates on the future of IgY technology. Included are a review of the potential application of IgY for the treatment of livestock diseases such as mastitis and diarrhea, poultry diseases such as *Salmonella*, *Campylobacteriosis,* infectious bursal disease and Newcastle disease, as well as aquatic diseases like shrimp white spot syndrome virus, *Yersina ruckeri* and *Edwardsiella tarda*. Some potential obstacles to the adoption of IgY technology are also discussed.

Contents

* Corresponding author at: School of Life Science and Technology, Dalian University of Technology, Dalian 116024, China. Tel.: +86 411 8470 6359; fax: +86 411 8470 6359.
E-mail address: jinliji@dlut.edu.cn (L. Jin).

0734-9750/$ – see front matter
doi:10.1016/j.biotechadv.2011.07.003

1. Introduction

Antibiotics have been used in animal agriculture for growth promotion (sub-therapeutic doses), disease prevention (prophylactic doses) and for the treatment of infection for over 50 years (Turner et al., 2001). Years of research and practical experience have shown that antibiotic use significantly improves animal performance and health status (Cromwell, 2002). However, the use and misuse of in-feed antibiotics have led to problems with drug residues in animal products and increased bacterial resistance (Khachatourians, 1998). As a result, the sub-therapeutic use of antibiotics has been totally banned in European countries since January 2006 (Casewell et al., 2003) and other countries are seriously considering a similar ban. Therefore, alternatives to antibiotics are urgently needed.

A wide range of products have been tested as potential alternatives to antibiotics including organic and inorganic acids (Kim et al., 2005), oligosaccharides (Flickinger et al., 2003), probiotics (Kritas and Morrison, 2005; Taras et al., 2007), herbal extracts (Windisch et al., 2008) and antibodies (Cook, 2004). Among these, oral immunotherapy (passive immunization) with antibodies is a highly attractive and effective alternative approach due to its high specificity. Oral administration with antibodies derived from mammalian serum and colostrum and even monoclonal antibodies have been used successfully (Kuhlman et al., 1988). However, with this technique, it is prohibitively expensive to obtain the large amount of antibody required to prevent and treat disease.

Recently, chicken egg yolk immunoglobulin, referred to as immunoglobulin Y (IgY) has attracted considerable attention as a means to prevent and control disease as it possesses a large number of advantages compared with treatment with mammalian IgG including cost-effectiveness, convenience and high yield (Carlander et al., 2000). Under natural conditions, the serum IgY of laying hens is deposited in large quantities in the egg yolk in order to protect the developing embryo from potential pathogens (Janson et al., 1995). Thus, it is possible to immunize the hen against specific foreign pathogens thereby allowing the production of IgY with activity against these specific disease conditions.

Oral administration of specific IgY antibody has been shown to be effective against a variety of intestinal pathogens such as bovine and human rotaviruses, enterotoxigenic *Escherichia coli* (ETEC), bovine coronavirus, *Salmonella* spp., *Edwardsiella tarda*, *Yersinia ruckeri*, *Staphylococcus* and *Pseudomonas* (Mine and Kovacs-Nolan, 2002). This review presents an overview of the potential to use immunotherapy with specific IgY for the prevention and treatment of terrestrial and aquatic animal diseases and speculates on the future of IgY technology.

2. Characteristics of chicken immunoglobulin Y (IgY)

2.1. Advantages of IgY

The use of chickens for the production of polyclonal antibodies provides many advantages over production methods using mammals (Table 1). The most significant advantage is that the collection of antibodies is non-invasive. In contrast to conventional methods where animals are often sacrificed in order to collect a sufficient amount of blood to obtain antibodies, production of antibodies in laying hens requires only the collection of eggs, and the high and long-lasting titers produced in chickens reduce the need for frequent booster injections. Another advantage is that due to the phylogenetic distance between chickens and mammals, chickens often more successfully produce antibodies against highly conserved mammalian proteins than do other mammals and require much less antigen to induce an efficient immune response.

A hen can be considered as a small "factory" for antibody production. A hen usually lays about 300 eggs per year and the egg yolk (15 ml) contains 50–100 mg of IgY of which 2 to 10% are specific antibodies (Rose et al., 1974). Therefore, one immunized hen produces more than 22,500 mg of IgY per year which is equivalent to the production of 4.3 rabbits over the course of a year (Schade et al., 2005). The maintenance costs for keeping hens are also lower than those for mammals such as rabbits (Schade et al., 2005). Therefore, egg yolk provides a more hygienic, cost-efficient, convenient and rich source of antibodies compared with the traditional method of obtaining antibodies from mammalian serum. In contrast to antibiotics, the use of IgY is environmentally-friendly and elicits no undesirable side effects, disease resistance or toxic residues (Coleman, 1999).

2.2. Structure and function of chicken IgY

Initially, IgY antibodies were thought to be similar to IgG immunoglobulins, whereas they are now considered to be an evolutionary ancestor to mammalian IgG and IgE and also to IgA (Warr et al., 1995). Although chicken IgY is the functional equivalent of mammalian IgG, there are some profound differences in their structure. The general structure of the IgY molecule is the same as the IgG molecule with two heavy (H) chains and two light (L) chains but IgY has a molecular mass of 180 kDa which is larger than that of mammalian IgG (150 kDa) (Fig. 1). The molecular mass (67–70 kDa) of the H chain in IgY is larger than the H chain from mammals (50 kDa). The greater molecular mass of IgY is due to an increased number of heavy-chain constant domains and carbohydrate chains (Warr et al., 1995). IgG has 3 C regions ($C_\gamma1$–$C_\gamma3$), while IgY has 4 C regions ($C_\upsilon1$–$C_\upsilon4$) and the presence of one additional C region with its two corresponding carbohydrate chains logically results in a greater molecular mass of IgY compared with IgG.

Other differences in structure include the fact that the hinged region of IgY is much less flexible compared with mammalian IgG. It has also been suggested that IgY is a more hydrophobic molecule than IgG (Davalos-Pantoja et al., 2000). Finally, IgY has an isoelectric point of pH 5.7–7.6, whereas that of IgG lies between 6.1 and 8.5 (Davalos-Pantoja et al., 2000; Sun et al., 2001).

Table 1
Comparison of the characteristics of mammalian IgG and chicken IgY.
Adapted from Schade et al. (2005).

Parameter	Mammalian IgG	Chicken IgY
Antibody sampling	Invasive	Non-invasive
Source of antibody	Blood serum	Egg yolk
Antibody amount	200 mg IgG/bleed (40 ml blood)	50–100 mg IgY/egg (300 eggs/year)
Frequency of collection	Every two weeks	Every day
Amount of antibody/year	5200 mg	22,500 mg
Amount of specific antibody	~5%	2–10%
Protein–A/G binding	Yes	No
Interference with mammalian IgG	Yes	No
Interference with rheumatoid factor	Yes	No
Activation of mammalian complement	Yes	No