

TECHNICAL LITERATURE

Immunoglobulin Y: Safety Evidence

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KEY CONCLUSIONS

- Immunoglobulin Y (IgY) is a water-soluble globular protein found in egg yolks.
- IgY content in egg yolk ranges from 45-150 mg.
- Based on USDA and Health Canada dietary guidelines on egg consumption, IgY intake in adults may be from 57-200 mg per day.
- No side effects from intake of IgY by animal and humans have been reported, supporting the safe use of IgY from eggs.
- IgY preparations may contain residual ovalbumin; therefore, caution should be taken when given them to egg-allergic individuals.

INTRODUCTION

Chicken eggs are known as good dietary sources of nutrients. There are three types of antibodies in chicken eggs: Immunoglobulin Y (IgY), IgA and IgM. Immunoglobulin Y, also known as γ -livetins, is a water-soluble globular protein found in egg yolk. It is transferred to the yolk by the hen to provide passive immunity to the developing chick. The other two immunoglobulins are found in the egg white[3].

Over the last 20 years, IgY antibodies have received significant attention as an economical and safe source of specific antibodies.

Source of IgY

The chicken egg is composed of approximately 9.5% shell, 63% albumin (egg white) and 25.5% egg yolk. The major constituents of the egg yolk are proteins, lipids and water. Within the protein fraction, 9.3 % are lipid-free, globular proteins called livetins. The relative percent of IgY (γ -livetins) in the protein fraction is about 3% (Table 1).

Table 1. Typical Composition of Chicken Egg Yolk[4-6]

Major Constituent	Amount, % (wet basis)	Relative % of components
Total solids	52.3-53.5	--
Protein	15.7-16.6	37.3% Apovitellenin (I-VI) 40.0% Lipovitellin apoproteins 9.3% Livetins (α -, β -, and γ -livetins 2:5:3[6]) 13.4% Phosvitin
Lipids	31.8-35.5	66% Triglycerol 28% Phospholipids 5.0% Cholesterol 1.0 % Others
Carbohydrates	0.2-1.0	0.2 % free carbohydrates ~0.8% protein-bound polysaccharides
Ash	1.1	Calcium, potassium and phosphorus

Adapted from Kovacs & Mine (2004) and Powrie & Nakai (1985)

Concentrations of IgY in egg yolk have been reported to range from 2.8-7 mg/mL to up to 10 mg/mL from non-immunized and immunized hens, respectively [7, 8]. Using an average egg yolk volume of 15 mL, these amounts represent 45-150 mg IgY/yolk.

Daily Consumption of IgY from Eggs

In 2011, the average annual per capita consumption of eggs in the U.S. was 248 eggs/person [9], or an average of 0.68 eggs/day. The typical weight of a medium size egg without the shell is ~ 1.6 oz (45 g), which corresponds to an annual per capita intake of ~ 1.1 oz (31 g) of edible egg per day.

According to the 2010 USDA dietary guidelines report, the average daily intakes of eggs by adults in the U.S. and Spain are 0.4 oz (11.3 g) and 1.9 oz (53.8 g), respectively[1]. If one assumes that a medium size egg contains an average of 100 mg IgY/egg, one could estimate the consumption of IgY by adults to be between 25-119 mg/d.

The most recent dietary guidelines from Health Canada and USDA recommend the consumption of not more than two eggs (~200 mg IgY) per day [2] and 4 egg yolks/ week (~57 mg IgY/d), respectively. The lower US guidelines are strictly based on the impact of egg consumption on total daily cholesterol intake [1].

IgY Physico-Chemical Properties

Immunoglobulin Y is the functional equivalent of mammalian IgG but it differs in many structural and physico-chemical properties (Table 2). Some of the differences include: higher molecular weight, the presence of four constant domains in the heavy chain, the lack of a flexible hinge region, an extra carbohydrate side chain in the Fc region and lower isoelectric point.

Immunoglobulin Y can be easily and non-invasively extracted from the chicken egg yolk at high concentrations (~40 g/year) and purities using various extraction processes. The choice of extraction process is determined by the final application[6]. Furthermore, IgY has also good stability to high temperature, pH, and freeze/spray drying conditions[6].

Table 2. IgY and IgG Structural and Physico-chemical Properties [4, 6]

Source of antibody	Avian IgY Egg yolk	Mammalian IgG Blood serum, cow milk & colostrum
Antibody yield per year	40,000 mg	1,400 mg
Molecular weight (kDa)	~180	~150
MW of heavy chain (kDa)	65-68	50
Heavy chain domains (#)	1 variable 4 constant	1 variable 3 constant
Flexible hinge region	No	Yes
Fc region carbohydrate side chains	2	1
Isoelectric point	5.4-7.6	6.1-8.5
Temperature stability (60-70 °C)	Stable	Stable
pH Stability (3.5 ≤ pH ≤ 11)	Stable	Stable

Due to the great phylogenetic differences between mammals and avian species, there is not immunological cross-reactivity between IgY and IgG [10]. The avian IgY neither activate the mammalian complement system nor bind the Fc mammalian receptors that could mediate inflammatory responses in the gastrointestinal tract [3].

Bioavailability of IgY from Eggs

Most of the knowledge on human bioavailability of immunoglobulins is based on research conducted with bovine milk IgG (BMG) and human serum IgG (HSG). In spite of the lack of pharmacokinetic data with IgY, numerous human studies using antigen-specific IgY have shown positive effects on passive immunity across a broad range of conditions. This suggests that either IgY or part of the antibody remains intact with capability to bind antigen after oral ingestion.

Immunoglobulins, in general, are thought to be more resistant to digestion than most common dietary proteins[11]. A human study with healthy adults consuming a ¹⁵N-labeled colostrum (bovine IgG) showed ~70% of IgG presence in the ileum. From the ingested IgG, 19% and 59% were still active in the ileum and the jejunum, respectively[12]. On the contrast, milk proteins are digested by 90-91% by the time they reach the terminal ileum[13]. Greater stability of immunoglobulins to digestion may be possible using microencapsulation technologies [14].

Orally administered HSG and BMG are not absorbed intact by either children[15] or infants [16, 17]. Furthermore, in healthy adults, intact immunoglobulins were not detected in their feces after oral intake of either 10 g HSG or 10 g IgY [18].

The current state of the science suggests that orally administered immunoglobulins may only be active locally, at the level of the mucosal surface. Furthermore, since no absorption of intact antibodies in humans has been shown, experts in the field believe that no systemic effects can be expected after oral administration of immunoglobulins to humans, including chicken IgY [10].

Studies with IgY

The use of antigen-specific IgY for passive immunization has been extensively studied in a wide variety of

animals models: mice, calves, pigs, dogs, rabbits, fish, shrimp, laying hens and broiler chicken[3, 6, 8]. In most cases, the IgY antibodies are administered in the animal feed in the form of whole egg powder, egg yolk powder, water-soluble fraction powder from the yolk or purified IgY[6]. The published studies show either a protective or preventive effect against specific pathogens. No side effects from the ingestion of IgY on all the above species have been reported, supporting the safe use of IgY derived from eggs.

In humans, antigen-specific IgY has been used in a variety of health conditions (Table 3)[8, 19]. No side effects have been reported.

Table 3. Published Human Studies with IgY

Study	Population treated	Dose (oral)	Length of supplementation	Adverse events
Good effect of IgY against <i>Pseudomonas aeruginosa</i> infections in cystic fibrosis patients[20]	17 patients	50 mg/d IgY	>12 years (114 patient years)	None reported
Oral administration of specific yolk antibodies (IgY) may prevent <i>Pseudomonas aeruginosa</i> infections in patients with cystic fibrosis [21]	17 patients	50 mg/d IgY	100 months	None reported
Effect of dietary anti-<i>Helicobacter pylori</i>-urease immunoglobulin Y on <i>Helicobacter pylori</i> infection[22]	17 healthy individuals	2.7 g/d Ovalgen (containing IgY)	4 weeks	None reported
Suppressive effect of functional drinking yogurt containing specific egg yolk immunoglobulin on <i>Helicobacter pylori</i> in humans[23]	21 healthy individuals	45 mg IgY/day	4 weeks	None reported
Randomized, placebo-controlled, clinical trial of hyperimmunized chicken egg yolk immunoglobulin in children with rotavirus diarrhea[24]	79 children	10 g of egg yolk (containing IgY) ^a	4 days	None reported
Increased muscular strength and enhanced muscle repair with hyperimmune egg protein supplementation[25]	12 healthy individuals	4.5-13.5 g/d egg protein powder (containing IgY) ^a	10 days	None reported
Hyperimmune egg protein decreases submaximal heart rate and increases peak power[26]	12 healthy individuals	4.5-13.5 g/d egg protein powder (containing IgY) ^a	10 days	None reported
Pilot study on the effect of hyperimmune egg protein on elevated cholesterol levels and cardiovascular risk factors[27]	15 healthy individuals	4.5-13.5 g/d egg protein powder	26 weeks	None reported
Administration to arthritis patients of a dietary supplement containing immune egg: an open-label pilot study[28]	13 patients	4.5 g powdered immune egg/d (containing IgY) ^a	8 weeks	None reported

^aNone of these studies reported the actual amount of IgY in their preparations.

Allergenicity of Chicken Eggs

Adverse allergic reactions to chicken eggs are caused by egg white proteins. Ovalbumin is the most predominant protein found in egg whites followed by ovomucoid, ovotransferrin, ovomucin and lysozyme[29]. The allergenic potential of IgY from eggs depends on the residual amounts of ovalbumin present in the final preparation. In a recent study, the trivalent seasonal influenza vaccine did not cause adverse reactions to egg-allergic children. The authors concluded that the use of the flu vaccine with very low residual amounts of ovalbumin (0.2 µg/ml) is safe in children with severe allergies to eggs [30]. Nevertheless, caution should be taken when giving IgY antibodies to egg-allergic individuals.

CONCLUSIONS

Immunoglobulin Y antibodies are globular proteins found in chicken eggs. Because of their unique properties, they have been widely used in research, diagnosis and passive immunization. The main dietary source of IgY is the egg yolk. The average consumption of IgY from eggs in adults may range from 25-200 mg/d depending on egg concentration and dietary behaviour. Numerous animal and human studies have been conducted with antigen-specific IgY extracted from egg yolks. Until now, no adverse events have been reported from orally administered IgY. However, caution should be exercised when providing IgY antibodies to egg-allergic individuals.

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