

# Potential food allergens in medications

John M. Kelso, MD *San Diego, Calif*

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**Overall Purpose/Goal:** To provide excellent reviews on key aspects of allergic disease to those who research, treat, or manage allergic disease.

**Target Audience:** Physicians and researchers within the field of allergic disease.

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**List of Design Committee Members:** John M. Kelso, MD  
**Activity Objectives**

1. To describe which food-derived substances are used as pharmaceutical excipients in which medications.
2. To review published data regarding the safety of administration of these medications to recipients with food allergy.
3. To prescribe these medications to most patients with food allergies.
4. To investigate potential allergy to the food component if a particular patient has had an apparent allergic reaction to a medication containing it.

**Recognition of Commercial Support:** This CME activity has not received external commercial support.

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**Companies/Organizations:** J. M. Kelso is a board member of the American Academy of Allergy, Asthma & Immunology (AAAAI); is employed by Scripps Clinic; and has received payment for lectures from the AAAAI, the American College of Allergy, Asthma & Immunology, the American Academy of Pediatrics, the American College of Physicians, and Symposia Medicus.

Excipients are substances in pharmaceuticals other than the active ingredients. Some excipients are foods or substances derived from foods, raising the possibility that these substances would pose a hazard to patients with food allergy. This review describes which food-derived substances are used as pharmaceutical excipients in which medications and reviews published data regarding the safety of the administration of these medications to recipients with food allergy. Such reactions are rare, usually because the amount of food protein is not present in a large enough quantity to elicit a reaction. When a food protein appears as an unintentional contaminant, the amount, if any, that is present might be variable and might elicit reactions only from some lots of medication or only in some patients. In most circumstances these medications should not be routinely withheld from patients who have particular food allergies because most will tolerate the medications uneventfully. However, if a particular patient has had an apparent allergic reaction to the medication, potential allergy to the food component should be investigated. (*J Allergy Clin Immunol* 2014;133:1509-18.)

**Key words:** Food allergy, medication allergy, vaccine allergy

### Abbreviations used

- IIV: Inactivated influenza vaccine
- ILE: Intravenous lipid emulsion
- LAIV: Live attenuated influenza vaccine
- TPN: Total parenteral nutrition

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Excipients are all of the substances found in pharmaceuticals other than the active ingredients. These substances are added to “aid the manufacturing process, to protect, support or enhance stability, or for bioavailability or patient acceptability.”<sup>1</sup> Some pharmaceutical excipients are foods or, more often, substances derived from foods, raising the possibility that these substances would pose a hazard to patients with food allergy.<sup>2</sup> The purpose of this publication is to describe which food-derived substances are used as pharmaceutical excipients in which medications (Table I)<sup>3-171</sup> and to review published data regarding the safety of the administration of these medications to recipients with food allergy.

Virtually all food allergens that generate IgE-mediated responses are proteins. In some cases the food excipients in medications are in fact proteins and thus capable of being allergenic. The amount and nature of (eg, how thoroughly hydrolyzed) these proteins might influence their allergenic potential. However, in many other cases the food excipient in the medication is a fat or carbohydrate and thus would not be expected to be allergenic. In these cases the excipient would have

From the Division of Allergy, Asthma and Immunology, Scripps Clinic.  
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Corresponding author: John M. Kelso, MD, Division of Allergy, Asthma and Immunology, Scripps Clinic, 3811 Valley Center Dr, San Diego, CA 92130. E-mail: [kelso.john@scrippshealth.org](mailto:kelso.john@scrippshealth.org).

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**TABLE I.** Potential food allergens in medicines

Food	Excipients	Drugs
Egg	Egg protein/ovalbumin	<ul style="list-style-type: none"> <li>Interferon Alfa-n3*</li> <li>Probiotics<sup>143</sup></li> <li>Vaccines<sup>3</sup>:               <ul style="list-style-type: none"> <li>influenza* (IIV,<sup>31-58</sup> LAIV)</li> <li>MMR*<sup>4-30</sup></li> <li>Rabies (PCEC)</li> <li>Yellow fever*</li> </ul> </li> </ul>
	Egg lecithin/phospholipids	<ul style="list-style-type: none"> <li>Emulsions:               <ul style="list-style-type: none"> <li>Clevidipine*</li> <li>Fat emulsions<sup>62,63</sup></li> <li>Propofol*<sup>64-81</sup></li> </ul> </li> <li>Tablets:               <ul style="list-style-type: none"> <li>Diphenhydramine</li> <li>Denofibrate</li> <li>Ibuprofen</li> <li>Multivitamin</li> <li>Rosiglitazone</li> </ul> </li> <li>Verteporfin injection<sup>82</sup></li> </ul>
Fish	Protamine	<ul style="list-style-type: none"> <li>Protamine injection*<sup>83-91</sup></li> <li>NPH insulin</li> </ul>
	Fish oil	<ul style="list-style-type: none"> <li>Fish oil supplements<sup>94</sup></li> <li>Some multivitamins</li> </ul>
Gelatin	Gelatin	<ul style="list-style-type: none"> <li>Many capsules and tablets<sup>97,98</sup></li> <li>Benzocaine oral gel</li> <li>Chloral hydrate suppositories<sup>99</sup></li> <li>Corticotropin repository injection</li> <li>Erythropoietin<sup>100</sup></li> <li>Hemostatic sponges<sup>101,102</sup></li> <li>Nicotine chewing gum</li> <li>Plasma volume expanders<sup>103-120</sup></li> <li>Sulfur colloid injection<sup>121</sup></li> <li>Vaccines<sup>3</sup>:               <ul style="list-style-type: none"> <li>Influenza (Fluzone,<sup>135</sup> FluMist*)</li> <li>Japanese encephalitis<sup>125,127,133</sup></li> <li>MMR*<sup>95,96,122,123,126,128,130,132,134,136,137</sup></li> <li>MMRV*</li> <li>Rabies (RabAvert)*</li> <li>Tick-borne encephalitis<sup>131</sup></li> <li>Typhoid vaccine, live oral</li> <li>Varicella*<sup>123,124,129,130,138</sup></li> <li>Yellow fever*</li> <li>Zoster*</li> </ul> </li> </ul>
Milk	Casamino acids	<ul style="list-style-type: none"> <li>Vaccines<sup>104,141</sup>:               <ul style="list-style-type: none"> <li>DTaP (Daptacel)</li> <li>DTaP-IPV/Hib (Pentacel)</li> <li>Meningococcal (Menomune)</li> <li>Pneumococcal (PCV13 – Prevnar 13)</li> <li>Td (Tenivac)</li> <li>Tdap (Adacel)</li> </ul> </li> </ul>
	Casein	<ul style="list-style-type: none"> <li>Cefditoren tablets*</li> <li>Miconazole tablets*</li> <li>Probiotics<sup>142</sup></li> <li>Vaccines<sup>140,141</sup>:               <ul style="list-style-type: none"> <li>DTaP (Infanrix)</li> <li>DTaP+HepB+IPV (Pediatrix)</li> <li>DTaP+IPV (Kinrix)</li> <li>Tdap (Boostrix)</li> <li>Typhoid (Vivotif)</li> </ul> </li> </ul>
	Cow's milk	<ul style="list-style-type: none"> <li>Some psyllium solutions</li> <li>Tums Smoothies tablets</li> </ul>
	Lactalbumin	<ul style="list-style-type: none"> <li>OPV<sup>143</sup></li> </ul>

(Continued)

**TABLE I.** (Continued)

Food	Excipients	Drugs
	Lactose <sup>144</sup>	<ul style="list-style-type: none"> <li>Many tablets, capsules, granules, and lyophilized powders<sup>145</sup></li> <li>Some psyllium solutions</li> <li>DPIs: device name (drug name/s)<sup>146-148</sup> <ul style="list-style-type: none"> <li>Aerolizer (Foradil)*</li> <li>Diskus (Advair, Flovent, Ventolin)*</li> <li>Flexhaler (Pulmicort)*</li> <li>HandiHaler (Spiriva)*</li> <li>Neohaler (Arcapta)*</li> <li>Pressair (Tudorza)*</li> <li>Rotahaler (Tiova)</li> <li>Turbuhaler/Turbohaler (Bricanyl, Oxis*, Pulmicort*, Symbicort*)</li> <li>Twisthaler (Asmanex)*</li> </ul> </li> </ul>
	Lactulose	<ul style="list-style-type: none"> <li>Lactulose solution<sup>149</sup></li> </ul>
Peanut	Peanut oil	<ul style="list-style-type: none"> <li>Dimercaprol injection*</li> <li>Progesterone capsules*</li> <li>Valproic acid capsules</li> </ul>
Pine nut	Rosen	<ul style="list-style-type: none"> <li>Fluoride tooth varnish<sup>150</sup></li> </ul>
Sesame	Sesame oil	<ul style="list-style-type: none"> <li>Dronabinol capsules*</li> <li>Estradiol injection</li> <li>Fluphenazine decanoate injection</li> <li>Haloperidol decanoate injection</li> <li>Nandrolone decanoate injection</li> <li>Progesterone injection*</li> <li>Testosterone injection</li> </ul>
Shellfish	Glucosamine	<ul style="list-style-type: none"> <li>Dietary supplements for arthritis<sup>151-156</sup></li> </ul>
	Iodine	<ul style="list-style-type: none"> <li>Radiocontrast media<sup>157</sup></li> </ul>
Soy	Soy lecithin	<ul style="list-style-type: none"> <li>MDIs<sup>161-166</sup> <ul style="list-style-type: none"> <li>Atrovent</li> <li>Combivent*</li> </ul> </li> </ul>
	Soy oil	<ul style="list-style-type: none"> <li>Emulsions:               <ul style="list-style-type: none"> <li>Clevidipine*</li> <li>Fat emulsions<sup>158-160,167-171</sup></li> <li>Propofol*<sup>64-81</sup></li> </ul> </li> </ul>
	Soy phosphatidylcholine	<ul style="list-style-type: none"> <li>Amphotericin B liposome</li> <li>Doxorubicin liposome</li> </ul>
	Soybean	<ul style="list-style-type: none"> <li>Tums Smoothies tablets</li> </ul>

Note that hundreds of nutritional supplements and homeopathic remedies not regulated by the US Food and Drug Administration also contain food ingredients. *DPI*, Dry powder inhaler; *MDI*, metered-dose inhaler; *MMR*, measles-mumps-rubella; *PCEC*, purified chick embryo cell.

\*The package insert lists food allergy as a warning or contraindication.

to be contaminated with protein for an allergen to be present. This type of contamination might well be random or variable. This variability in the amount and nature of food protein present in medications by design or by accident means that there could be great lot-to-lot variability in the presence of these proteins. Individual patients would also be expected to vary quite widely in susceptibility to allergic reactions with exposure to these food proteins in medications, depending on the amount of IgE antibody generated against the particular food allergen and particular epitopes on the food allergen.

## EGG

### Egg protein/ovalbumin

**Vaccines.** Measles, mumps, and purified chick embryo cell rabies vaccines are grown in chick embryo fibroblast cultures and

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