Carol Rees Parrish, R.D., M.S., Series Editor

Medications and Celiac Disease—Tips From a Pharmacist

Steven Plogsted

Celiac disease is a chronic, generically linked, autoimmune disorder that is also known as celiac sprue, nontropical sprue, and gluten-sensitive enteropathy. Although celiac disease primarily affects the small intestine, deleterious effects can occur throughout the entire body. Patients with celiac disease are unable to tolerate the ingestion of gluten. Gluten is an insoluble protein found in all cereal grains. The gluten that is found in wheat, rye, and barley is the offending culprit for celiac disease patients. The prevalence in the United States is estimated to effect 1% of the population. The following article is designed to help identify medications that may contain gluten.

INTRODUCTION

Patients who have been diagnosed with celiac disease (CD) or have a need to follow a gluten-free (GF) diet must be aware of potential sources of gluten. In the area of pharmaceuticals, potential sources of gluten contamination come primarily from the addition of the excipient (filler) ingredients added to the active drug in order to make a particular dosage form.

Steven Plogsted, Pharm.D, BCNSP, Clinical Pharmacist, Nutrition Support Service, Columbus Children's Hospital, Clinical Assistant Professor of Pharmacy, Raabe College of Pharmacy, Ohio Northern University, Columbus, OH.

Gluten ingestion in a patient with Celiac Disease causes an immunologically mediated inflammatory response, which results in damage to the mucosa of the small intestine. It requires only a relatively small amount of the gluten to illicit this response so it is important to avoid the exposure (1,2).

Excipients form the bulk of the product and are designed to perform several functions. In addition to providing bulk, they may be utilized as lubricants for the powder, or as in the case of starches, absorb water, which causes the tablet to swell and disintegrate. It is these starches that provide the potential source of gluten contamination. These excipients can be obtained from any starch source, but are primarily derived from

(continued from page 60)

THE CELIAC DIET, SERIES #5

(continued from page 58)

Table 1
Common Excipient Ingredients in Medications

Benzyl alcohol	made synthetically from benzyl chloride which is derived from toluene (a tar oil)
Cellulose	(methylcellulose, hydroxymethylcellulose, microcrystalline, powdered)—obtained from fibrous plant material (woody pulp or chemical cotton)
Cetyl alcohol	derived from a fat source (spermaceti, which is a waxy substance from the head of the sperm whale)
Croscarmellose sodium	an internally cross-linked sodium carboxymethylcellulose for use as a disintegrant in pharmaceutical formulations. It contains no sugar or starch.
Dextrans	sugar molecules
Detrates	mix of sugars resulting from the controlled enzymatic hydrolysis of starch
Dextrins	result from the hydrolysis of starch (primarily corn or potato) by heat or hydrochloric acid. It can also be obtained from wheat, rice or tapioca
Dextri-maltose	A sugar that may be obtained from barley malt
Dextrose	A sugar that is obtained from corn starch
Fructose	A sugar also known as levulose or fruit sugar
Gelatin	Obtained from the skin, white connective and bones of animals (by boiling skin, tendons, ligaments, bones, etc with water)
Glycerin	Historically, glycerin (also known as glycerol), was made the following ways: • Saponification (a type of chemical process) of fats and oils in the manufacturing of soaps • Hydrolysis of fats and oils through pressure and superheated steam • Fermentation of beet sugar molasses in the presence of large amounts of sodium sulfite • Today it is made mostly from propylene (a petroleum product)
Glycerols	obtained from fats and oils as byproducts in the manufacture of soaps and fatty acids (may also be listed as mono-glycerides or di-glycerides)
Glycols	products of ethylene oxide gas
Iron oxide (rust)	used as a coloring agent
Kaolin	A clay-like substance
Lactilol	Lactose derivative
Lactose	Lactose, or milk sugar, is used in the pharmaceutical industry as a filler or binder for the manufacture of coated pills and tablets
Maltodextrin	A starch hydolysate that is usually obtained from corn but can also be extracted from wheat, potato or rice
Mannitol	derived from monosaccharides (glucose and mannose)
Polysorbates	chemically altered sorbitol (a sugar)
Povidone (crospovidone)	synthetic polymers
Pregelatinized starch	A starch that has been chemically or mechanically processed. The starch can come from corn, wheat, potato or tapioca
Shellac	A natural wax product used in tablet or capsule coating
Sodium lauryl sulfate	derivative of the fatty acids of coconut oil
Sodium starch glycolate	A starch that is usually obtained from potato but may come from any starch source
Stearates (calcium, magnesium)	derived from stearic acid (a fat; occurs as a glyceride in tallow and other animal fats and oils, as well as some vegetables; prepared synthetically by hydrogenation of cottonseed and other vegetable oils)
Sucrose	Refined sugar also known as refined sugar, beet sugar or cane sugar

Table 1 (continued)

Titanium dioxide	chemical not derived from any starch source used as a white pigment
Triacetin	derivative of glycerin (acetylation of glycerol)
Silcon dioxide	dispersing agent made from silicon

corn, potato and tapioca; however, they have also been known to contain starch from wheat. There are a few products that are clearly labeled as GF, however, the majority of the manufacturers do not provide that information on either the package or the package insert.

ROLE OF THE FOOD AND DRUG ADMINISTRATION

The United States Food and Drug Administration (FDA) is responsible for overseeing the safe manufacturing of drug products. While they maintain strict regulations for the active ingredient of the drug product, they provide minimal over-site for what excipients can be added. The drug manufacturers must utilize only FDA approved excipients, but the quantity and type of excipient is not specifically regulated. This is important to understand, especially in the manufacturing of generic drug products, *since generic product does not have to contain the same excipients as the brand name product.* The generic drug manufacturers must demonstrate certain absorption characteristics when they reproduce a drug, but all other aspects can differ.

WHEN TO CALL THE DRUG MANUFACTURER

Where can a consumer or health care professional obtain the necessary drug information? Can this information be trusted? The consumer or health care professional needs to consider two questions when an inquiry is made about the gluten content of a drug. The first question is what are the inactive ingredients or excipients? Excipients are listed in the package insert and should be the first place a pharmacist looks for information (Table 1). Once the excipients are read the second question that should be asked is, what is the source of the ingredient? Again, the package insert provides the pharmacist with the starting point. One of the first key words to look for in the inactive ingredients section is *starch*. As mentioned previously, starch can be derived from several sources including corn, potato, tapioca, and wheat. If the product lists starch as "cornstarch" or "starch (corn)" it can be assumed to be GF. If starch by itself is listed, a call to the manufacturer is the ***only way*** to confirm the source of the starch. Other common terms include pregelatinized starch and sodium starch glycolate. Both products are starches derived from corn, wheat, potato, or rice, however, they have been chemically treated or processed. Despite manipulation, some gluten can remain, although it is unlikely.

There are also the four "Dex-ingredients" derived from starch (dextrans, dextrose, dextrates, dextrins). Dextrans come from corn and potato starch; dextrose comes from corn. These Dex-ingredients are not a problem for CD patients. Dextrates and Dextrins can come from *any* starch source so a call to the manufacturer is the only way to know if it contains gluten. It is important to know that other ingredients are derived from wheat, but are not hazardous because of the process in which they are made; conversely, just because a product is processed does not mean all gluten has been removed. For instance, some alcohols are derived from wheat. Because the alcohol is purified, the alcohol contains no protein (gluten) making it safe for CD patients. On the other hand, a product may originally start without glutens, but in the manufacturing process, may become cross-contaminated. This is exactly the reason that a pharmacist should call the manufacturer as the second step even after reviewing the inactive ingredients in the package insert. This step should be taken as a safeguard whenever possible. Patients with CD often receive education about the GF diet from a dietitian because they are the experts in the field. It is the same case with medications. Pharmacists are the experts in drug information, which includes knowing if excipients contain gluten. Patients are referred to pharmacists for that information just like they are referred to dietitians to get information about diet. Unfortunately, many pharmacists are not well-versed enough about CD and the

Table 2
Gluten Free Pharmaceuticals Resources*

Glutenfree Drugs	http://www.glutenfreedrugs.com
Stokes Pharmacy	http://www.stokesrx.com
Clan Thompson	http://www.clanthompson.com
Celiac Sprue	A Guide Through the Medicine Cabinet, by Marcia Milazzo http://www.celiacmeds.com
Wheaton Gluten Free Support Group	http://homepage.mac.com/sholland/celiac/GFmedlist.pdf

*The GF status of medications should be confirmed by periodically contacting the manufacturer.

gluten content of medications to be able to answer questions received from CD patients.

HOW YOUR PHARMACIST CAN HELP

Pharmacists may often be called upon to determine whether a pharmaceutical product is GF. This can be a challenging task. In a survey performed in 2001, only five of 100 pharmaceutical companies had a policy ensuring gluten-free status for their medications, although many more stated that *they believed* their products to be GF (3). One of the problems faced by the pharmaceutical manufacturers is the uncertainty of the GF status of the raw materials obtained from outside sources. Cross contamination during manufacturing can also occur. A reliable way of determining the GF status of the medications that a CD patient is taking is essential to the health of the CD patient. Several books and web sites are available to assist in this process, but should be thought of as starting places (Table 2). If possible, inquiries should be made directly to the pharmaceutical companies to ensure the GF status of a particular product. Adding to the burden of the CD patient is the fact that pharmaceutical manufacturers frequently change the inactive ingredients of their products. This can happen without warning, so the GF status of a product should be re-assessed on a regular basis. Any indication that a product is "new and improved," "new formulation," "new product appearance," or "new manufacturer" should be a sign that the GF status of the product must be reestablished.

One of the most common problems encountered when trying to obtain the gluten status from the drug manufacturer is the manufacturers lack of information. They often will respond that they don't use any gluten in the manufacturing of their product, but because they buy raw materials (excipients) from outside sources they cannot verify that those excipients are GF. While there is no way to know if a product is GF, having an understanding of the excipients' origin or how those excipients are produced, the pharmacist can provide an educated assessment of the *likelihood* of gluten contamination. We still need to contact the manufacturers and we can usually trust the information they give us when they state that their product is GF. The ultimate choice to take the medication, however, lies with the consumer.

Information for prescription medications are more plentiful than for over-the-counter (OTC) drugs. The government controls are not as tight for OTC drugs on the market; information regarding the gluten status is often difficult to obtain and less reliable. The consumer should always try to find a source for these products in anticipation of need. The Walmart® chain, for example, displays the gluten status of many of their OTC products directly on the package (see Table 3 for common GF OTC medications).

Fortunately, nutritional supplements are now under the new Food Allergen Labeling and Consumer Protection Act of 2004 that went into effect in January 1, 2006 and must be labeled if they contain wheat (barley and rye are not used in the preparation of medications.) The Act further directs the Food and Drug Administration (FDA) to develop and implement a plan on GF labeling within the next two years as well as defining the term "gluten-free" for labeling purposes for food products but not medications (4).

Developing a relationship with your local pharmacist is one way to make access to drug information timelier and less intimidating. Although pharmacists are experts in their knowledge of medications, they may not be as familiar with CD or how the excipients are produced. Taking the time to explain your condition and even point them to various sources of information can be helpful. It is important to understand the

(continued on page 64)

THE CELIAC DIET, SERIES #5

(continued from page 62)

Table 3
Common Over-the-Counter Gluten Free Products

Actifed
Advil Cold and Sinus
Alavert (all forms)
Aleve
Alka Seltzer Gold
Aspirin Enteric Coated 325mg (Leiner,code #44/227, Watson)
Aspirin 81mg chewable (Watson)
Baby aspirin (Walgreens, Perrigo)
Bugs Bunny Chewables
Chlortrimeton 4 mg tabs
Chlortrimeton 8mg and 12 mg extend tabs
Chlortrimeton liquid
Codiclear DH (sugar and dye free)
Comtrex (tabs/caplets/liquid)
Comtrex Deep Chest Cold
Comtrex Non Drowsy
Freeda's Vitamins
Ibuprofen (manufact. is Pharm Formulations)
Kirkman (all products are GF)
Motrin Childrens DF Conc. Drops
Mobic
Morphine Sulfate Ext Release Tab (Endo)
Motrin (Children's) oral susp
Motrin Cold DF Berry
Motrin DF Oral Susp Berry
Motrin IB caplets
Motrin IB tabs
Mucinex (all forms)
Nature Made brand multivitamins
Natures Plus Animal Parade
Pepto Bismol
Robitussin Cold & Congestion Caplet
Robitussin Cold & Cough Liqui-Gels
Robitussin Cold Severe Congestion liqui-gels
Robitussin Cold, Cough & Flu Liqui-Gels
Robitussin line
Robitussin Multi Symptom Cold & Flu Caplets
Robitussin Night Time liqui-gels
Sesame Street Complete Vitamins & Minerals
Slo-Mag
Sudafed
Sudafed Cold & Sinus Liquid Caps
Sudafed Plus
Twin Lab Animal Friends Multivit wafers
Twin Lab Animal Parade Cherry
Ultramega Gold (GNC)
Viactiv
VitaminShoppe brand all GF

Table 4
Summary of Key Points

1. Gluten can be found as a normal component of a drug product. When a product contains the word "starch" the source should be identified. Corn, rice, potato and tapioca starch are safe for celiac patients.
2. While all product formulations should be checked with the manufacturer, it is not always possible to do so in a timely manner.
3. The likelihood of gluten contamination is small for products that do not contain excipients derived from starch.
4. The product package insert is a good place to start in search for gluten in medications, but may not completely answer the question.
5. Internet resources may also provide some help, but caution should be taken regarding this source.

time constraints pharmacists are under; allowing them to obtain this information during non-peak hours will increase their level of cooperation. For more resources on GF medications, see Table 2.

CONCLUSION

Obtaining accurate information regarding the gluten status of medications and over-the-counter products can be a difficult and time-intensive process. Lack of understanding of what gluten is and how gluten can filter into our lives is a barrier to retrieving this information. Proper education of the health care professional can be a valuable tool in combating this problem. For a summary of key points, see Table 4. ■

References

1. Anon. National Institutes of Health Consensus Development Conference Statement. Celiac Disease, 2004; June 28-30.
2. Fasano A, Berti I, Gerarduzzi T, et al. Prevalence of celiac disease in at-risk and not-at-risk groups in the United States: a large multicenter study. *Arch Intern Med,* 2003;163: 286-292.
3. Crowe JP, Falini NP. Gluten in pharmaceutical products. *Am J Health-Syst Pharm,* 2001; 58:396-401.
4. Pietzak M. Gluten-free Food Labeling in the United States. *J Ped Gastroenterol Nutr,* 2005;41:567-568.