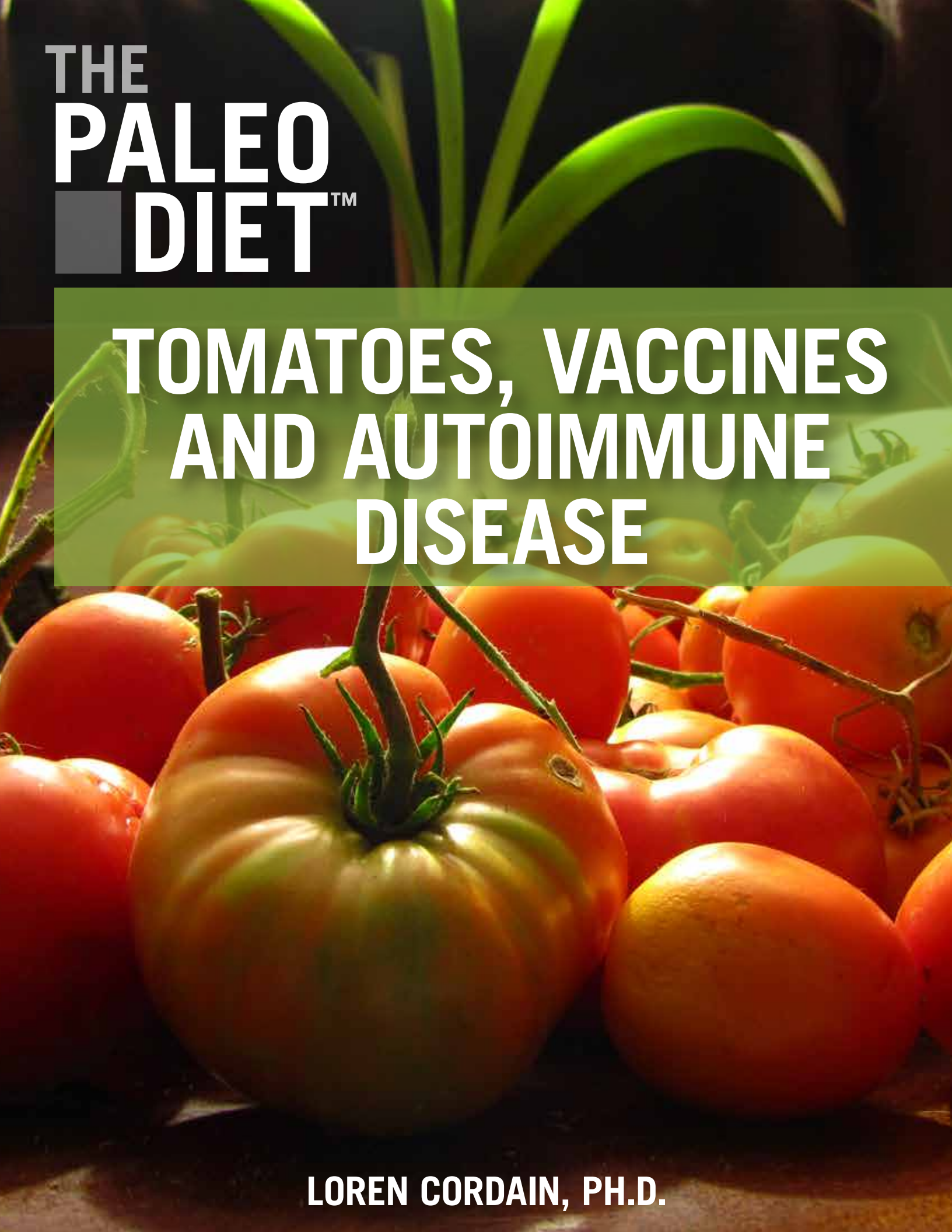
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TOMATOES, VACCINES AND AUTOIMMUNE DISEASE
LOREN CORDAIN, PH.D.

TOMATOES, VACCINES, AND AUTOIMMUNE DISEASE

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After cardiovascular disease and cancer, autoimmune diseases are the most common class of illnesses in the U.S., afflicting between 14.7 to 23.5 million people or 5 to 8 % of the entire population.[1] By far, the burden of these diseases disproportionately involves women, who sustain 78.8 % of all cases of autoimmune diseases.[2]

Further these diseases collectively fall among the top 10 leading causes of death for women in every age group up to age 64.[3] More than 80 specific diseases are known to be autoimmune in nature, and you probably recognize a few of the more common ones listed in the table below.

Table 1. Common autoimmune diseases.

Disease	Tissue/Organ Affected	Prevalence
Alopecia areata	Hair follicle	170 per 100,000
Ankylosing spondylitis	Spine and sacroiliac joints	129 per 100,000
Autoimmune urticaria	Skin	330 per 100,000
Celiac disease	Small intestine	400 per 100,000
Crohn's disease	Gastrointestinal tract	184 per 100,000
Diabetes (type 1)	Pancreas	120 per 100,000
Graves' disease	Thyroid gland	1120 per 100,000
Hashimoto's thyroiditis	Thyroid gland	9460 per 100,000
Lupus erythematosus	Any tissue in the body	510 per 100,000
Multiple sclerosis	Central nervous system	140 per 100,000
Psoriasis	Skin	2020 per 100,000
Rheumatoid arthritis	Joints	920 per 100,000
Scleroderma	Skin, many other organs	110 per 100,000
Sjögren's syndrome	Salivary and tear glands	370 per 100,000
Ulcerative colitis	Colon	35 to 100 per 100,000
Uveitis Anterior	Eye	850 per 100,000
Vitiligo	Skin	740 per 100,000

Autoimmune diseases develop when the body's immune system loses the ability to distinguish between what is "self" and what is "non-self" and attacks healthy tissues and organs as if they were a foreign invader. Approximately 30% of the risk for developing an autoimmune disease is attributed to your genes, but far and away, environmental factors are much more important in determining who ultimately winds up with a full blown autoimmune disease and who doesn't.[1]

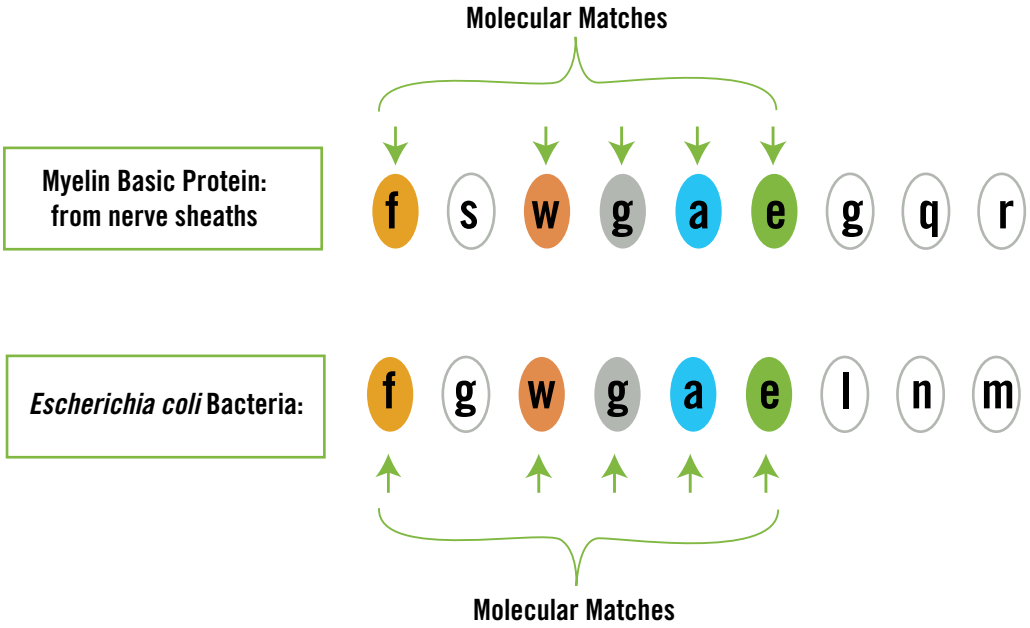
Various environmental factors are suspected in eliciting autoimmune diseases in genetically predisposed individuals including drugs, heavy metals, ultraviolet radiation exposure, wheat gluten ingestion and viral and bacterial infections.[1] Of the common autoimmune diseases (Table 1), infectious agents such as viruses and bacterial are thought to be the most likely environmental trigger.[1] How viruses and bacteria ultimately set off an autoimmune response is not completely understood, but many scientists[4-6] including myself [7] believe it is through a process called molecular mimicry whereby amino acid sequences from viruses and bacteria resemble amino acid sequences in our body's organs and tissues (see Figure 1).

This similarity in molecular structure between infectious agents and our body's own tissues sometimes confuses certain components of the immune system causing "self tolerance" to break down, thereby resulting in the destruction of tissues and organs by the immune system.

Exposure to viruses, bacteria and other microbes most typically occurs in a number of ways: 1) the microbe may enter your body through mucous membranes in your nose, mouth or gastrointestinal or genitourinary tracts, or 2) it enters your body through a break in your skin caused by a wound or insect/vector bite. On a daily basis, we are regularly exposed to microbes via all of these pathways, however far and away the greatest regular exposure to microbes comes from viruses and bacteria that reside in our intestines.[8] In healthy, normal people the gut tissue represents a powerful barrier that prevents microorganisms within the gut from entering the bloodstream. Additionally, certain components of the immune system and the liver act to prevent proteins (antigens) from gut microbes from entering circulation. However, under certain circumstances gut permeability may increase thereby facilitating the first step for entry of microbe antigens and food antigens into circulation.[7]

An emerging consensus among scientists who study autoimmune disease is that a number of autoimmune diseases (including type 1 diabetes, Crohn's disease, dermatitis herpetiformis, rheumatoid arthritis, celiac disease, and ankylosing spondylitis) have an environmental trigger that originates from a leaky gut thereby allowing microbe and food antigens continual access to the immune system.[7,9,10] Before I can address how tomatoes may be involved in this whole process, I've got to briefly explain how vaccines work.

Figure 1. Schematic representation of the molecular mimicry process.



The immune response is normally a healthy reaction because it allows our bodies to detect foreign antigens derived from invading microbes and take appropriate steps by the immune system to destroy these organisms. Medicine has taken advantage of this naturally occurring response and has utilized it to prevent diseases in the form of vaccines.

With a typical vaccine, killed or weakened microorganisms are injected into the body with a hypodermic needle and syringe. The immune system then recognizes the vaccine antigens as foreign and destroys them, and in the process learns to "remember" them. When the "real" or virulent version of the vaccine antigen appears, the immune system recognizes the invading microbe and destroys it thereby preventing the disease. With an autoimmune disease, it is as if this very same process occurs, except that the immune response is directed at one or more of the body's own tissues or organs.

Before we move on to tomatoes and autoimmune disease, I've got to bring up another concept: adjuvants. When immunologists first began to make vaccines they realized that many vaccines, simply didn't work with weakened viruses or bacteria alone. They simply didn't rev up the immune system sufficiently to result in a full blown immune response. It was eventually discovered that by mixing the weakened or killed microbe with another compound called an adjuvant the effectiveness of the vaccine was increased and full immunity could be established.

The three most commonly used adjuvants are 1) alum (aluminum hydroxide), 2) Freund's adjuvant and 3) Complete Freund's adjuvant. Of these three, only alum is licensed for human use; the other two are used primarily in animals.

So from what I've explained, you might expect it possible for scientists to cause autoimmune diseases by creating vaccines containing some of the body's own tissues (antigens). Clearly, it would be unethical to deliberately cause an autoimmune disease in humans, but experiments in animals confirm that organ specific autoimmune diseases can be caused by injecting a self antigen with a powerful adjuvant such as Complete Freund's.[11, 12] Neither the adjuvant alone nor the self-antigen typically results in autoimmunity in animals.[2, 11, 12] Now the question arises, is it possible that we can unknowingly be exposed to "natural" vaccines (containing pathogens plus adjuvants) that trick our immune systems into developing immunity against our own tissues?

As immunologists further developed vaccines, instead of injecting the foreign antigen with a hypodermic needle through the skin, they attempted to initiate an immune response by having subjects swallow a capsule containing the foreign antigen. Invariably, these experiments failed because dendritic cells in the gut which normally process foreign antigens did not elicit an immune response, but rather were un-reactive. This un-reactive state by dendritic cells is actually the normal or default response and is called oral tolerance and prevents immune responses to non-harmful dietary and microbial antigens. Immunologists discovered that if they administered the foreign antigen containing capsule along with an adjuvant, they could now prevent oral tolerance by dendritic cells and cause a full blown immune response.[13-15] So if a gut borne antigen is simultaneously present with a gut borne adjuvant, the state is set for promoting an immune response that may lead to an autoimmune response if molecular mimicry exists between the gut borne antigen and one of the body's own tissues.

In the wild world of the internet, urban legend has it that consumption of nightshade (tomato, potato, eggplant, bell peppers, hot peppers, and paprika) free diets may improve symptoms in some rheumatoid arthritis patients.[16] Is there any scientific basis for these alleged anecdotal observations?

In order for any food protein (antigen) to potentially cause or promote an autoimmune disease, it must:

1. Survive the human digestive processes intact

2. Cross the gut barrier intact either alone or with other attached proteins (antigens)

3. Interact with the immune system in a manner suspected of causing an autoimmune disease.

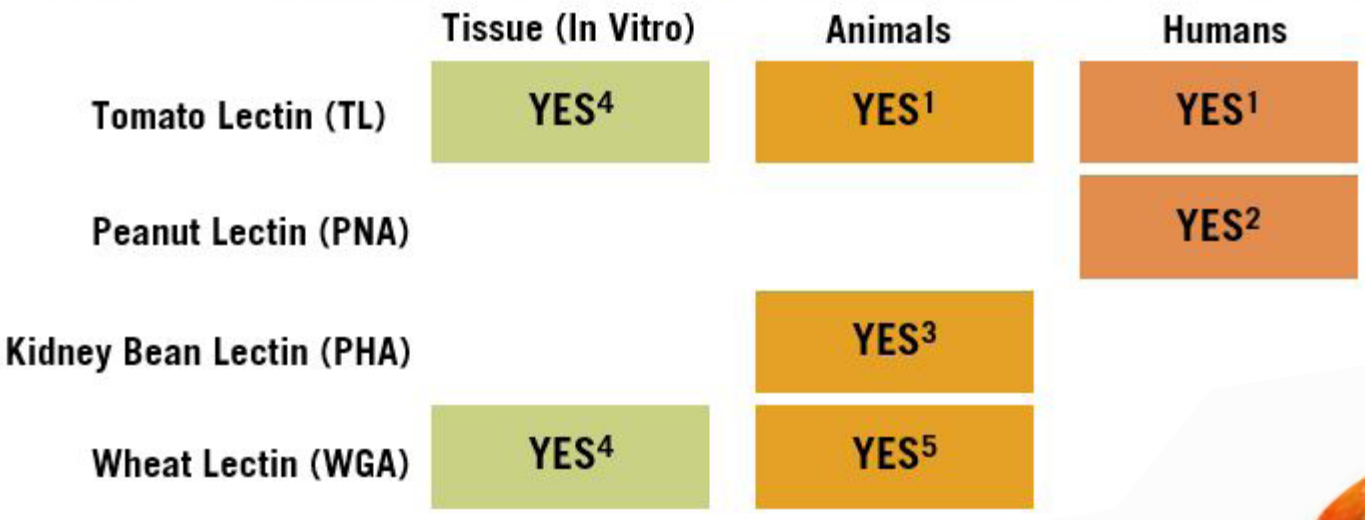
At least one naturally occurring compound found in tomatoes (tomato lectin) fulfills all three of the above requirements. Tomato lectin is present in the fruit and leaves of tomato plants and its primary function is to prevent predation by insects, fungi, viruses and bacteria.[17] If you take a look at Figure 2 below, you can see that tomato lectin rapidly ends up in the bloodstream of both humans and animals following ingestion of either tomatoes or tomato juice.

Although it is not known with certainty how tomato lectin breeches the gut barrier and gains access into circulation, it most likely does so through a back door pathway called the epidermal growth factor receptor (EGF-R). The EGF-R is a highly unusual receptor because it faces the gut contents[18] which are, in effect, the outside of the body. Normally hormonal receptors face the bloodstream where they can bind their specific blood borne hormones. Tomato lectin, like all lectins, binds specific sugars, and this is how it attaches itself to the EGF-R because of it's specificity for sugars contained on the surface of the EGF-R. The lectin found in wheat (WGA) likely gains access to circulation because it binds the EGF-R.[19] Not only does tomato lectin bind the EGF-R, but it also binds bacteria and viral antigens in the gut that have sugar specificities to tomato lectin. Hence, tomato lectin has the capacity to drag gut antigens into circulation in a Trojan horse like manner as depicted in Figure 3 below.

Once in the gut lining, the tomato (lectin/microbial antigen) complex is picked up by dendritic cells which can then migrate to the lymph and then into circulation where this complex is presented to circulating white blood cells (T cells). As I mentioned earlier, the normal dendritic cell response is not to elicit an immune reaction, but rather oral tolerance. That is except if an adjuvant is simultaneously present.

Well, you guessed it; tomatoes contain not only tomato lectin, a vehicle for gut borne antigen delivery into circulation[20], but also a powerful adjuvant called alpha tomatine[21] which has been consistently demonstrated to elicit immune responses in dendritic cells.[22-28]

Figure 2. Dietary lectins known to breech the gut barrier and arrive intact in circulation.



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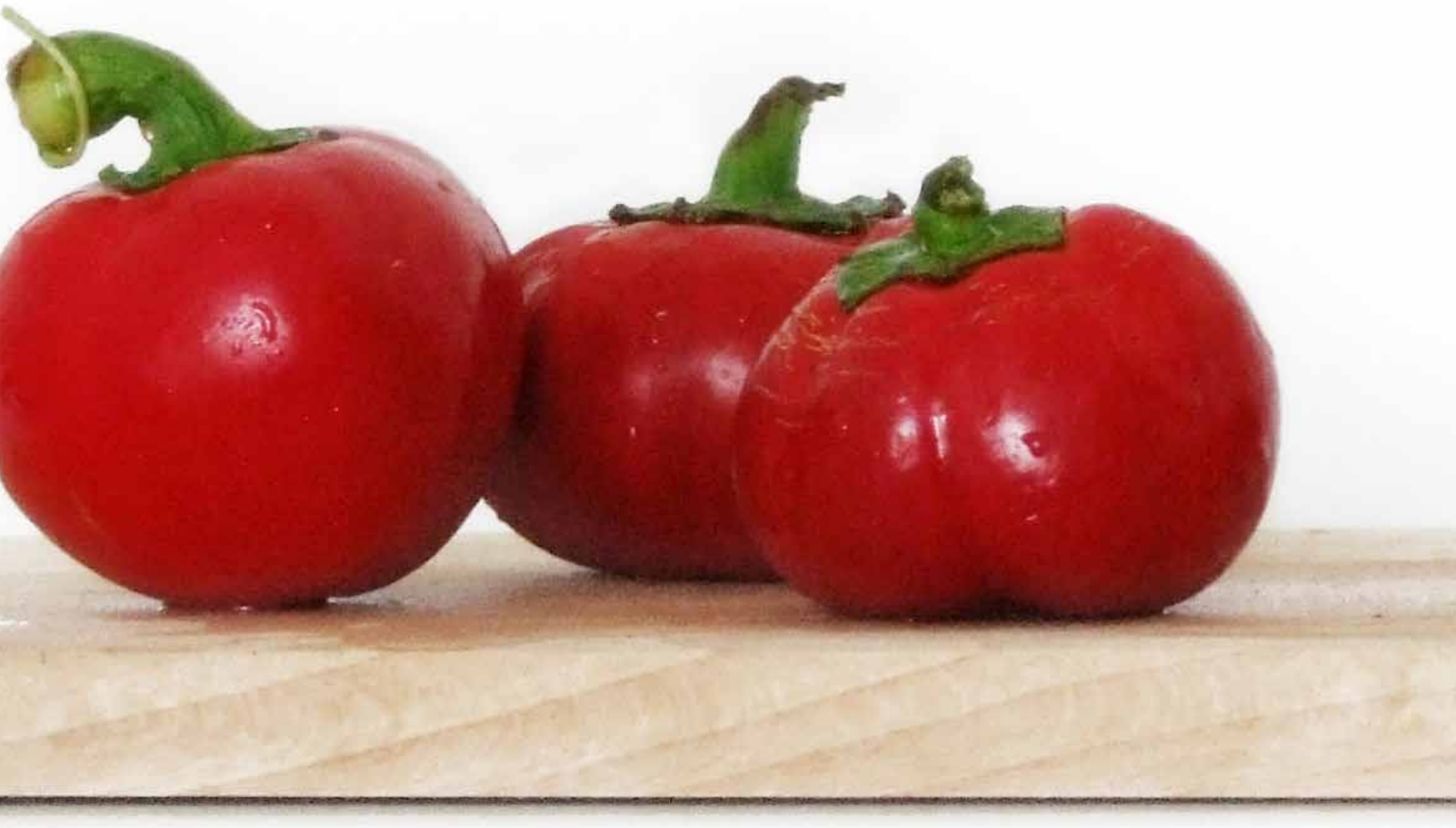
Alpha tomatine is technically called a saponin, substances which can cause an immune response at extremely low doses.[29, 30] The alpha tomatine content declines in tomatoes as they ripen with the highest concentrations found in green tomatoes.[31] Green salsas, cherry tomatoes and ketchup also contain relatively higher concentrations of alpha tomatine than ripe red tomatoes.[31]

Because alpha tomatine is a saponin, it also increases intestinal permeability and likely accelerates the leakage of gut borne antigens into circulation via the paracellular (between cell) pathway.[32, 33] Further the combination of a dietary lectin with a saponin represents a double whammy because it creates an additive effect upon gut permeability.[34] The saponin breeches the gut barrier via the paracellular pathway[32-34] while the lectin probably uses both a transcellular receptor mediated pathway (e.g. the EGF-R) and a paracellular route.[35-36]

So the bottom line is that tomatoes contain two substances that are routinely used in the manufacture of vaccines, an adjuvant (alpha tomatine) and an immunogen (tomato lectin/microbial antigen complex). Hence, in theory, there likely is a scientific basis for the use of nightshade free diets in the treatment of rheumatoid arthritis[16] and other autoimmune diseases. To date, there are no animal or human experiments that confirm or deny this hypothetical evidence. As has been my policy in the past, I believe that anyone suffering from an autoimmune disease should remove suspect foods from the diet for an extended period and then monitor symptoms. If conditions get worse after you re-introduce the food, then this particular food may be problematic for you and should not be part of your lifelong diet. I would add tomatoes to my short list of cereal grains, legumes, dairy products, yeast containing foods, and eggs.



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