The Real Skinny on Green Light Therapy

This is a dry read…but try and make it through! I've underlined a couple of sentences that I really want you take in.

1. Overview. Current phototherapy for acne is primarily done with red lamps emitting at 630 nm and blue lamps emitting at 420 nm. This project relates to using green lamps emitting primarily at 546 nm (550 nm). The main purpose in light therapy for treating acne is to use the energy of the light to excite a chromophore produced by the P. acnes bacteria. This chromophore is called coproporphyrin III or CP-III.

When light excites CP-III in the presence of molecular oxygen, the molecular oxygen absorbs triplet state energy of the excited (photosensitized) CP-III to form singlet oxygen which is a highly reactive form of molecular oxygen. This highly reactive singlet oxygen then interacts with structures inside the bacteria (mainly lipid membranes) to kill the bacteria. The process is called photodynamic therapy or PDT.

2. Why light works. The simplistic view of photodynamic therapy is that if the light matches the absorption spectrum of the chromophore then the procedure should work well. If light doesn't match the absorption spectrum of the chromophore then the amount of excited chromophore will be low and the PDT effect will be low.

In reality the PDT mechanism requires that three things be together in the body at the same time. These three things are oxygen, chromophore (photosensitizer), and light.

Generally the amount of molecular oxygen is the limiting factor. The next limiting factor is usually the amount of photosensitizer. The amount of light (assuming the wavelength is right) is usually, but not always, the third limiting factor.

If the light is well absorbed by the photosensitizer molecule (CP-III in the case of acne) and more than 50 mw/cm2 is delivered to the skin, the result is nearly instantaneous hypoxia in the tissue. In other words the available oxygen is immediately consumed and after the first seconds of irradiation there is no oxygen left to perform the PDT. It is crucial that this oxygen be replaced, and normally this is done by a slow diffusion process from the blood supply, or in some cases there is direct diffusion of oxygen from the air through the skin.

Blue light cannot penetrate the skin effectively. The working depth of penetration of blue light at 420 nm is 0.25 mm (0.010”). The limited amount of blue light that reaches past the epidermis is quickly absorbed by the blood in the soret band. Blue light cannot reach the 1-4 mm depth of acne bacteria. Almost all of blue light at 420 nm is absorbed by chemicals in the epidermis and this light never makes it to the CP-III inside the bacteria a

very shallow depth of bacteria are killed. The blue light is absorbed by melanin, retinoic acids, guanylate cyclases, P450 cytochromes, bilirubin, protophorphyrins, etc. in the epidermis. Although blue light phototherapy gives good results, it does not give GREAT results, mostly due to the absorption in the epidermis.

Green light penetrates much further past the epidermis and reaches into the papillary dermis where there is a large volume of blood. In general the papillary dermis contains 10X the amount of blood needed to service the tissues in this area. The reason for this is to provide cooling for the body.

This large reservoir of blood is also a large reservoir of oxygen if we can release the oxygen from the blood. Green light from 540 nm to 560 nm does this. This process called photodissociation releases oxygen from oxyhemoglobin and thereby acts as a new source of tissue oxygen. The photodissociation process for green light is very efficient (about 15% quantum efficiency) and this provides reoxygenation of the tissue.

Since oxygen is the primary limiting factor in PDT, we can use green light to increase the oxygen content of the tissue thus raising the efficiency of the PDT by an order of magnitude. This cannot be done with blue light (limited depth of penetration). Red light can photodissociate the oxygen from the oxyhemoglobin, but it is not very well absorbed. It takes 70 times as much red light at 630 nm

as green light at 550 nm to photodissociate the same amount of oxygen from oxyhemoglobin.

Green light at 540 nm –560 nm acts as an oxygen source for the oxygen-driven PDT reaction. It is a mini-hyperbaric chamber applied to the skin.

3. Photosensitization. Although CP-III absorbs very well at 400-430 nm (the Soret band) very light blue light can reach deep enough into the skin to activate CP-III. Green light at 550 nm reaches much deeper, liberates oxygen, and is the second highest absorption peak of CP-III. Given that blue light cannot reach deep enough to get to the CP-III produced by the bacterial, the highest absorption peak from a clinical standpoint is at 546 nm. The bandwidth is fairly broad as indicated in the graph located at the end of this discussion.

4. Green Light Non-Interaction. The body is a complex set of chemicals, many of which are interacting with light energy at different levels. If we view PDT as the interaction of a given wavelength of light with CP-III (or other photosensitizer) it is important to look at the other interactions that are occurring simultaneously. For example, blue light is absorbed by a large number of molecules. Blue light doesn't reach deep enough to photosensitize CP-III very well, but it does get absorbed. One of the absorbers of blue light is a chemical called all-trans retinoic acid. Blue light destroys all- trans retinoic acid through a photooxidation process. The

maximum photodestruction occurs at 420 nm. All-trans retinoic acid is the major chemical in the skin that helps control acne inflammation (through it's effects on TLR2 receptors on cells).

Perhaps the worst effect of any light source to treat acne would be to reduce all-trans retinoic acid, and blue light is the worst possible wavelength.

We observe the effects of green light at 550 nm and it is not absorbed by all-trans retinoic acid, so we are not removing this crucial chemical by green light. For phototherapy, we need to assess not only what photobiological responses we want, we have to search for those reactions we wish to avoid. The selection of 550 nm was based on its ability to generate oxygen, its excellent absorption by CP-III at a reasonable skin depth, and its ability NOT to create other difficulties when administered to the skin.