Phototoxic?

- Development of a screening model -

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- Supervision by assoc. prof. Jens Spanget-Larsen, RUC
- Possibility for experimental work at LEO Pharma A/S
- Become acquainted with a pharmaceutical company and learn how optical spectroscopy is applied extensively in the medical industry

Phototoxicity!

– What is this and why is it important? -

Anyone who suffers from some kind of eczema (Fig. 1) or an inflammation skin illness like psoriasis (Fig. 2) knows how troublesome it is. It itches, hurts, and looks definitely unattractive! For these persons it is of great importance, physically as well as mentally, that efficient and safe medical treatments are developed which can relieve or remove the unpleasant symptoms. Most treatments are based on application directly on the skin of the active ingredient formulated as a crème or a gel. By development of new drugs it is very important that these drugs are not phototoxic.

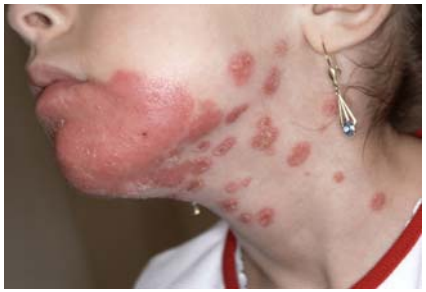

Figure 1. Eczema

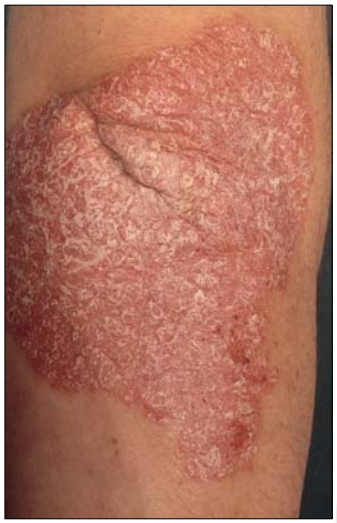

Figure 2. Psoriasis

Phototoxicity is a light-induced, nonimmunologic, skin response to a photoreactive substance.

Phototoxicity is initiated by the absorption of light. Photochemical reactions in the excited molecule may lead to formation of free radicals (Type I photo-dynamic reaction) or singlet oxygen, $^1O_2$ (Type II photodynamic reaction). Alternatively, the excited molecule may react directly with other molecules, which, *e.g.*, may lead to formation of covalent bonds to DNA or skin proteins, or to the formation of toxic photoproducts. Most phototoxic compounds react through one of the two photodynamic mechanisms and absorb light with wavelengths between 290 and 700 nm (Fig. 4).

The Project

- collaboration with LEO Pharma A/S -

Traditionally, phototoxicity is testet by *in vitro* screening in cell-based assays. But this is a complicated and costly procedure, and it is not sufficiently reliable.

It would be of great interest if *in vitro* screenings could be supplemented by a ”dry model”, which on the basis of spectroscopic, chemical, and structural data and the results of theoretical calculations could predict whether a given compound is likely to exhibit phototoxic properties. It is the purpose of this project to investigate the possibility for development of such a model.

The availability of an efficient ”screening model” would be of substantial importance for the pharmaceutical industry. Too late discovery of the phototoxic properties of a drug candidate may be a very expensive business.

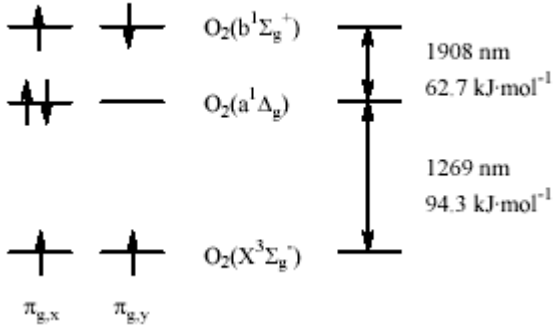

Figure 3. Orbital diagram of the lowest electronic states of oxygen. The diagram shows the distribution of the two electrons in the highest occupied, degenerate molecular orbital (HOMO).

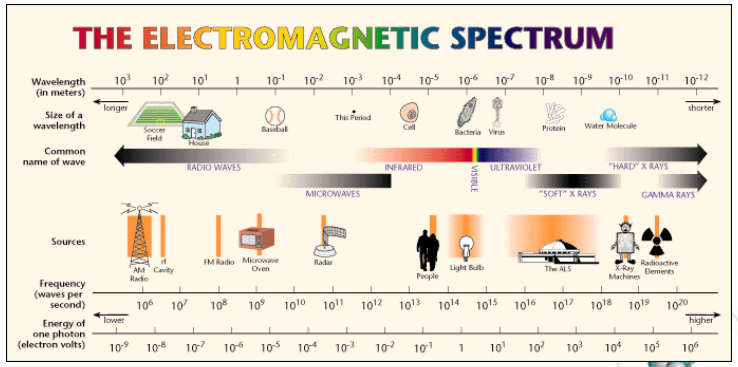

Figure 4. The electromagnetic spectrum.