PHOTOACOUSTIC TECHNIQUE APPLIED TO *IN VIVO* SKIN RESEARCH

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PURPOSE OF THIS WORK

The purpose of this work is to present the various applications of the photoacoustic (PA) technique in skin research and transdermal drug delivery studies performed through *in vivo* measurements in healthy humans.

INTRODUCTION

Photoacoustic (PA) effect (Graham Bell, 1880):

Production of sound waves as a consequence of modulated (pulsed) light absorption:

Modulated light → Heat → Periodic Expansion/Contraction → Acoustic waves

Applications of the PA Technique:

Study of biological systems and processes:

- Caracterization of **biomaterials** (human skin, teeth, artificial skin, biological tissues)
- **Sunscreens** analysis
- **Drug delivery** studies (topically applied products)
- Other: Photosynthesis measurements, polymerization of dental resins

EXPERIMENTAL METHODS

The experimental setup employed at the ***Laboratory of Photoacoustics Applied to Biological Systems*** includes a tungsten lamp (250W) or a xenon lamp (1000W) as light sources; lock-in amplifier (SRS, mod.SR530), mechanical chopper (SRS, mod.SR540); lenses, a double-sided PA cell (developed at UNIVAP, with an internal electret microphone) and a microcomputer for data acquisition. A monochromator is employed in PA spectroscopy measurements.

In vitro measurements have been performed in VitroSkin® samples. For *in vivo* measurements, skin is gently pressed against the open end of the PA cell.

As radiation is absorbed by the sample, the heat generates acoustic waves detected by the microphone. As the PA signal depends on optical and thermal parameters of the sample, it can be used to determine the characteristics of the skin itself or topically applied products, as well as kinetic changes related to transdermal drug delivery.

After recording the PA signal for the clean skin, the product under analysis is applied (through massage or phonophoresis) on the sample. The PA signal is then recorded at regular intervals, up to a total time of the order of the process under study (*circa* 30 minutes for anti-inflammatory drugs; up to 6h for sunscreens).

Fitting curves – PA measurements as a function of time (as in drug delivery, dehydration and rehydration studies) are normally adjusted by a Boltzmann equation or an exponential decay. Both allow the determination of the "typical time constant" of the process/product under study.

RESULTS

Absorption spectra for skin, sunscreen and for the bilayer system "skin+sunscreen" were obtained through PA spectroscopy (Fig.1). Also, pigmentation skin level was qualitatively determined through direct *in vivo* PA measurements (data not shown).

Transdermal drug delivery has been evaluated through PA data as a function of time after topical application of different drugs in the forearm region, using manual massage or phonophoresis (see example in Fig.2). Results show that different products present distinct absorption times (depending on the vehicle employed, for example). The application method also affects the typical time constant of drug penetration into skin, though not for all tested formulations.

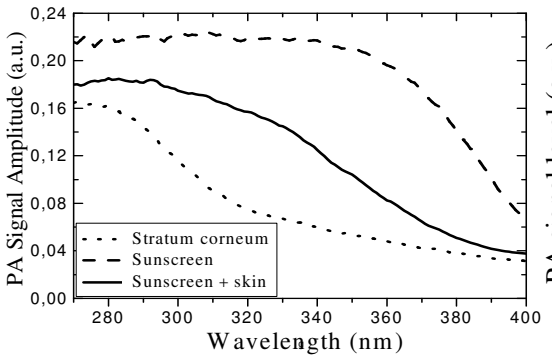

Fig. 1. Absorption spectra of skin (stratum corneum) and sunscreen.

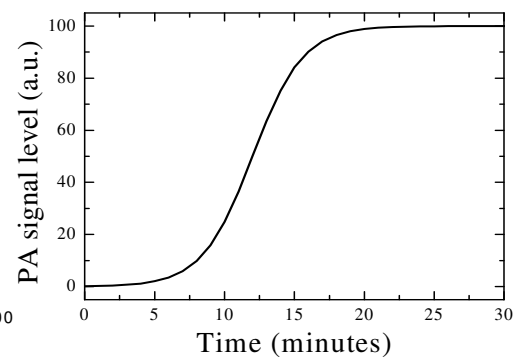

Fig.2. Fitting curve for the PA signal as a function of time after phonophoresis applications (average curve for Nimesulid gel).

CONCLUSIONS

- The PA technique has been sucessfully employed particularly in **drug delivery** studies, demonstrating for example in which cases phonophoresis can help drug delivery through skin
- In most cases, PA measurements show that the **excipient** employed in formulation is decisive for the typical time constant of the product (with gel formulations accelerating penetration).
- The results obtained show the usefulness of the Photoacoustic Technique in skin research; next steps in this field may include *in vivo* **PA spectroscopy** measurements in humans.

The author acknowledges Fapesp for financial support (JP 04/02193-1)