

Current topics of Autoradiography in New Drug Development Studies of Japan

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The 116 annual meeting of the Pharmaceutical Society of Japan was held in Kanazawa from March 27 to 29 in 1996. Our presentation will be concerned to a few topics in this meeting. Recently not only pharmaco- and toxico-kinetic studies but also pharmaco- and toxico-dynamic studies are beginning to be worthy of notice. This is quite reasonable, because the blood concentration-time curves of a parent compound must be useful, but it is no more than a cross section for pharmaco- and toxico-dynamics in many organs and tissues as main reaction site for drug metabolism.

Autoradiography data have been used not much as an efficient evidence in this field in the past, in comparison with HPLC data because of their less quantitation than other analytical methods. Since 1988, the above established theory has been lost by the advent of "Quantitative recording and displaying instrument of 2 dimensional radiation image" —Bioanalyzer system (BAS series).

The advent of a new tool has been producing some epochmaking application manners for pharmaco- and toxico- dynamic studies.

And the spread of the above instrument brought several informations concerning advantages and disadvantages of the conventional autoradiography techniques. This presentation will touch the above problems.

Materials and Methods

Two dimensional ^{14}C standard source, Raytest in Germany, was used for calibrating thickness and its self-absorption of thin whole body sections. Two kinds of rat whole body sections (30 and 50 mm in preset, thickness) were provided in this experiment; one was non-labeled body and the other was ^{14}C -labeled body.

The most sensitive radiation sensor, Imaging Plate, IP, was substituted for a X-ray film. Non-labeled rat organs and tissues were prepared in accordance with the frozen microautoradiographic procedure.

The frozen thin sections were mounted on a nuclear emulsion plate, previously provided by an Appleton method, in a dark room for a suitable exposure period. After photoprocessing, the thin sections contacted with developed silver grains were stained by a hematoxylin-eosin method. A part of the thin sections was contacted with a IP for recording and displaying of BAS imaging.

Results and Discussions

The data noticed that some necessary considerations would be necessary for presenting any kind of quantitative autoradiographic data.

Problems were pointed out in the following procedures: freezing-, sectioning-, picking the sections up and mounting it on a sticky tape and freeze-drying.

When a non-labeled thin organ or tissue section was contacted with IP, it was certainly that there was no autoradiographic image. However, our experimental data indicated that in many microautoradiographic examples by a direct contact method, Appleton's method, remarkably positive image was revealed on non-labeled tissues or organs; — so called as a chemical fogging reaction. In addition to this, some hypersensitization phenomenon also was observed on the developed nuclear emulsion.