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MEDICAL DIVISION
DEPARTMENT OF
CLINICAL INVESTIGATION
OFFICE OF
HAROLD A. TUCKER, M.D.

October 28, 1959

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Upjohn
Board
Conrad
October 28 1959

Doctor Lee E. Farr
Medical Director
Brookhaven National Laboratory
Upton, New York

Dear Doctor Farr:

I read with interest your article in the current issue of Science, and it seemed likely that some of the people on your staff might be intrigued by a recent development in the psoralen area. Briefly, there is some evidence that whatever is present in tissues after the ingestion of methoxsalen somehow interacts with roentgen energy, as it had previously been shown to do with mid and near ultraviolet.

In the hope that some of your people may be interested, I enclose several items. "Psoralens and Radiant Energy" gives a solid background picture of the furocoumarins, particularly in relation to U. V. Zimmerman does report grenz ray studies (page 270), suggesting that such energy produces effects similar to those obtained with U. V., i.e., "photosensitization."

On the other hand, C. M. Levin, using 200 KV, HVL 1.6 mm. Cu., reports what appears to a primary protective, or skin-sparing effect of the drug. He has since treated 12 additional patients, using methoxsalen prior to all treatment sessions, in some cases 30 or more, with even more obvious increase in tolerance. He also reports using one patient as her own control, with striking differences in the skin areas.

Finally, in Abstract 38,765, Kawamoto, et al., describe a controlled study in which leukemia occurred with much greater frequency in mice given total body x-radiation without the drug (72.2%) than in those receiving the drug in the diet (5.0%). A chemical leukemogen was equally damaging in control and treatment groups, suggesting a specific interaction between the roentgen energy and the psoralen.

Methoxsalen has been used for many years, but surprisingly little research worthy of the name has been done with it. We do know that it is widely distributed in foodstuffs, (parsley, celery, parsnips, figs, citrus fruits, etc.) and our experience has shown it to be nontoxic (as would be expected).

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If there is a real protective effect against the untoward activities of electromagnetic energy in the roentgen band, one should be able to prove it, and to find out whether effects of more penetrating energies might also be modified. But such proof might require uncommon ingenuity and "know how," as well as instrumentation not widely available. Your description of the Brookhaven medical research reactor suggested that your group might well wish to study this problem, even though the data at this juncture are admittedly fragmentary.

I welcome your comments.

Sincerely yours,

THE UPJOHN COMPANY

Harold A. Tucker

Harold A. Tucker, M. D.

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Enclosures 3

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Subject: Methoxsalen and Other Psoralens

38,765
(Rev.)

The Effect of Oxypsoralen upon Leukemogenesis in Mice by
X-Rays and Methylcholanthrene

1959

Kawamoto, Sadahisa; Kirschbaum, Arthur; Taylor, Grant (Section of Pediatrics,
The University of Texas M. D. Anderson Hosp. and Tumor Inst., Houston,
Texas)

Texas Repts. Biol. & Med. 17:341-344 (Fall) 1959

Adding methoxsalen to the diet of 6-week-old mice (0.5 Gm. of methoxsalen per kilogram of feed) for 10 months had the following effects upon the induction of leukemogenesis and skin carcinogenesis in these animals, which were observed for a total of 18 months:

- (1) did not protect DBA/2 male mice against induction of leukemia with methylcholanthrene
- (2) did not inhibit the induction of skin carcinogenesis by methylcholanthrene in DBA/2 male mice
- (3) significantly protected against the leukemogenic effect of x-irradiation (x-rad.) in C57BL mice, as follows:

<u>Treatment</u>	<u>No. of mice developing leukemia</u>	<u>Per Cent</u>	<i>Statistically significant if controlled properly etc.</i>
Whole body x-rad.*	8 of 9 females } 5 of 9 males } 13 of 18	72.2%	
Whole body x-rad. plus dietary methoxsalen	1 of 10 females } 0 of 10 males } 1 of 20	5%	
Dietary methoxsalen	0 of 8 females } 0 of 10 males } 0 of 18	0%	

*Whole body x-irradiation was given in 11 doses at 4-day intervals, each dose consisting of 80 r.

There was no evidence that weight loss was induced by the ingestion of methoxsalen.

jkm/ldl

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