

From

ICI Pharmaceuticals Division 22 OCT 1971

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To

Your ref

Our ref PFCB/CN Tel ext

Date 20th Oct

Dear

ICI 63197 - USE AS AN EMETIC IN PARAQUAT FORMULATIONS

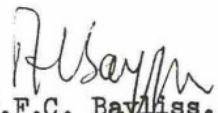
Thank you for your letter of the 7th October upon the above topic.  
I would like to make the following observations:-

- 1) ICI 63197, although definitely emetic, does not have a clearly defined emetic dose, and therefore it would be difficult to choose a dose which could be guaranteed to produce vomiting in all individuals, unless it is a very high dose.
- 2) Besides producing vomiting, at a higher dose it produces marked cardiovascular changes, which I really consider to preclude its use as a simple emetic.
- 3) Even when vomiting does occur, it is usually after 15 minutes; also by which time I would imagine that more than a toxic dose of paraquat will have been absorbed, either through the mouth or through the stomach. The evidence is that ICI 63197 is a central rather than a local emetic, and thus does not cause immediate vomiting.
- 4) You suggest that ICI 63197 might be too expensive. I am afraid that I do not know how expensive it is likely to be, and this is of course made even more difficult because it is still at a very early stage of development.
- 5) You ask what tests are used here for an emetic effect. In fact we are not searching for an emetic, and therefore there are no primary tests designed to this end. However, a compound which is emetic will usually show up in most animals which are capable of producing antiperistalsis. Laboratory dogs seem particularly sensitive to foreign substances and vomit at least provocation, so in fact there is a high incidence of apparent emesis from simple observations of laboratory animals.

In conclusion, I feel that ICI 63197 is not suitable for the indication you suggest, and on general prospects, I suspect that the inclusion of an emetic in paraquat is unlikely to be of much benefit, because of the extremely rapid absorption of paraquat that can occur in the mouth.

If you want to pursue this matter further, you might like to phone me.

Yours sincerely,

  
P.F.C. Bayliss.

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