

EXHIBIT A



US006790966B2

(12) **United States Patent**
Romanczyk, Jr. et al.

(10) **Patent No.:** US 6,790,966 B2
(45) **Date of Patent:** Sep. 14, 2004

(54) **COCOA EXTRACTS CONTAINING SOLVENT-DERIVED COCOA POLYPHENOLS FROM DEFAITED COCOA BEANS**

6,627,232 B1 * 9/2003 Hammerstone, Jr.
et al. 424/776

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(*) **Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) **Appl. No.:** 10/342,772

(22) **Filed:** Jan. 15, 2003

(65) **Prior Publication Data**

US 2003/0176493 A1 Sep. 18, 2003

Related U.S. Application Data

(60) Continuation of application No. 09/975,242, filed on Oct. 11, 2001, now Pat. No. 6,517,841, which is a continuation of application No. 09/768,473, filed on Jan. 24, 2001, now Pat. No. 6,562,863, which is a continuation of application No. 09/172,873, filed on Oct. 15, 1998, now Pat. No. 6,225,338, which is a division of application No. 08/839,446, filed on Apr. 14, 1997, now Pat. No. 5,891,905, which is a division of application No. 08/687,885, filed on Jul. 26, 1996, now Pat. No. 5,712,305, which is a division of application No. 08/317,226, filed on Oct. 3, 1994, now Pat. No. 5,554,645.

(51) **Int. Cl.**⁷ **A23F 5/00**; A23G 1/00; C07D 309/00; C07D 313/00

(52) **U.S. Cl.** **549/354**; 549/355; 549/396; 426/302; 426/542; 426/593; 426/631

(58) **Field of Search** 549/354, 355, 549/386; 426/302, 542, 593, 631

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(57) **ABSTRACT**

Disclosed and claimed are cocoa extracts such as polyphenols or procyanidins, methods for preparing such extracts, as well as uses for them, especially as antineoplastic agents and antioxidants. Disclosed and claimed are antineoplastic compositions containing cocoa polyphenols or procyanidins and methods for treating patients employing the compositions. Additionally disclosed and claimed is a kit for treating a patient in need of treatment with an antineoplastic agent containing cocoa polyphenols or procyanidins as well as a lyophilized antineoplastic composition containing cocoa polyphenols or procyanidins. Further, disclosed and claimed is the use of the invention in antioxidant, preservative and topoisomerase-inhibiting compositions and methods.

24 Claims, 91 Drawing Sheets

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FIG. 1

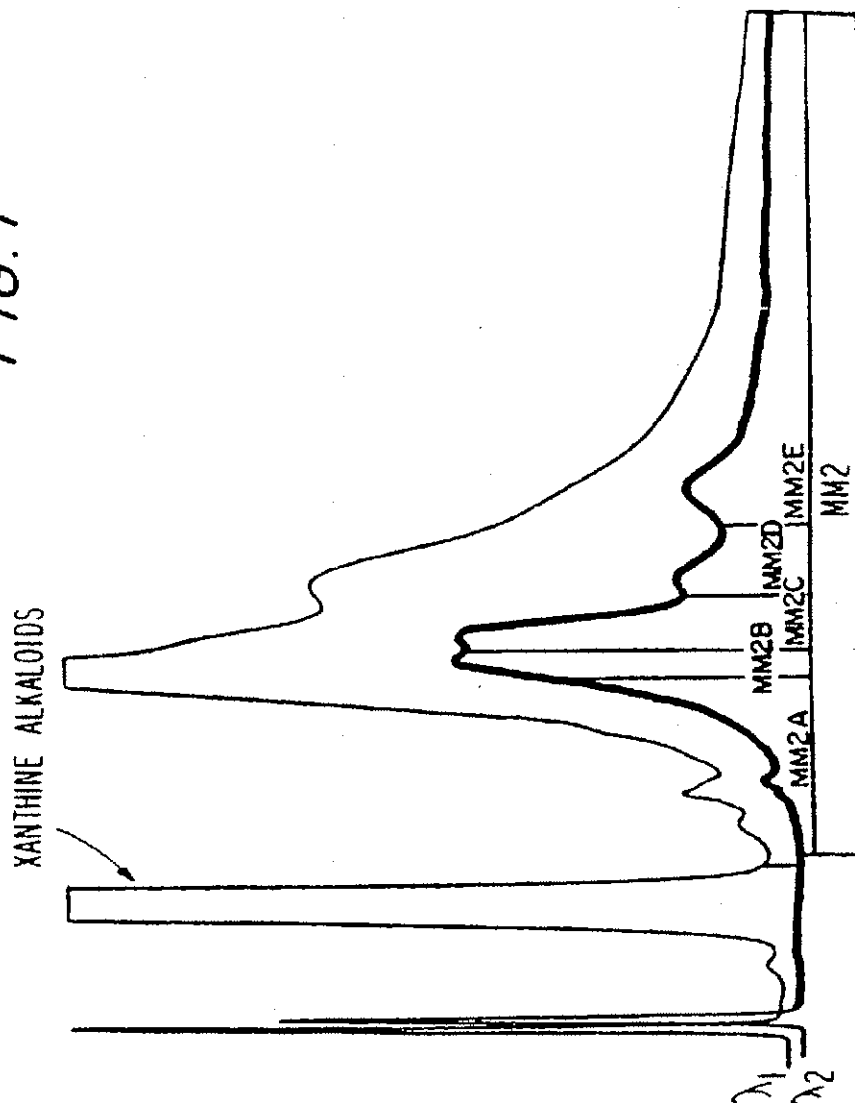
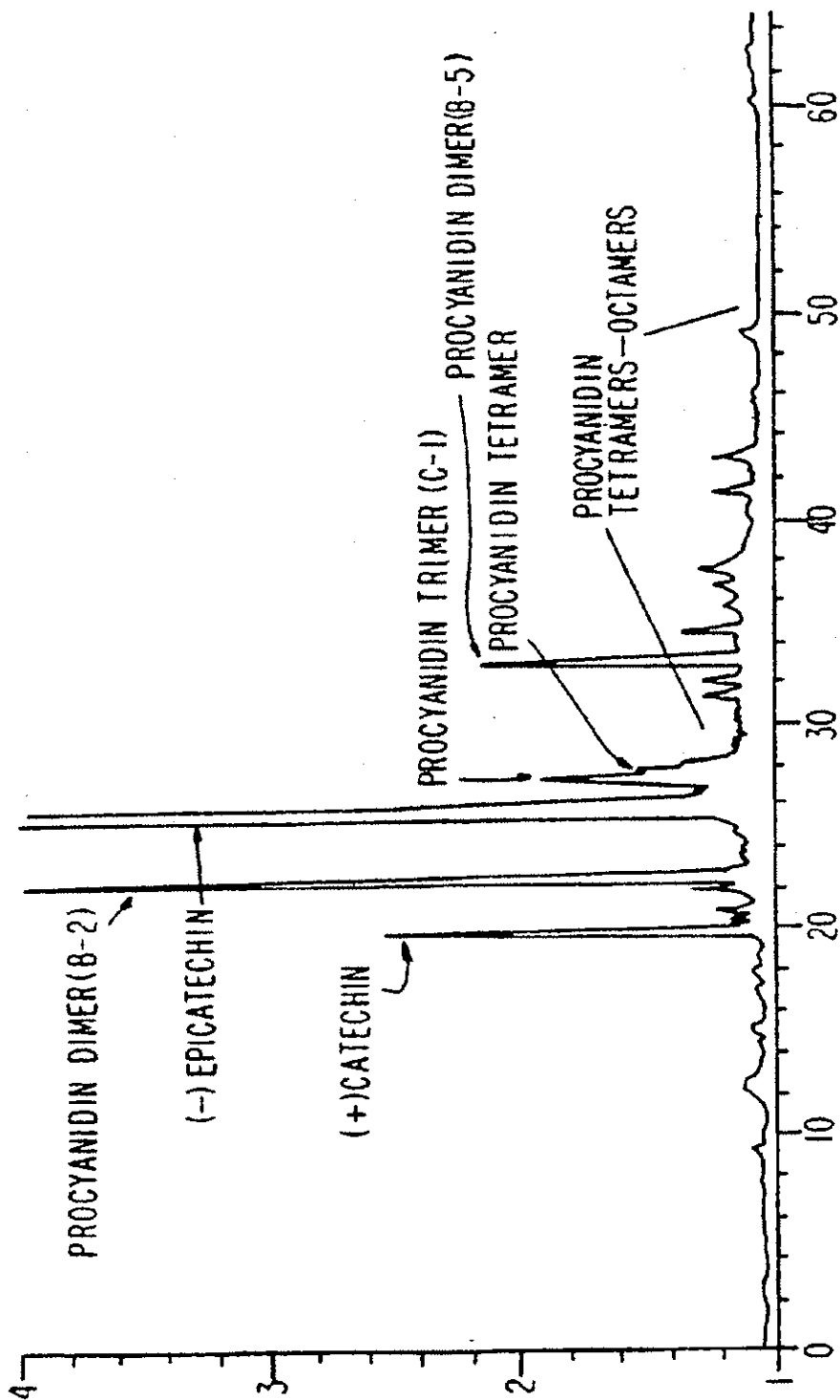
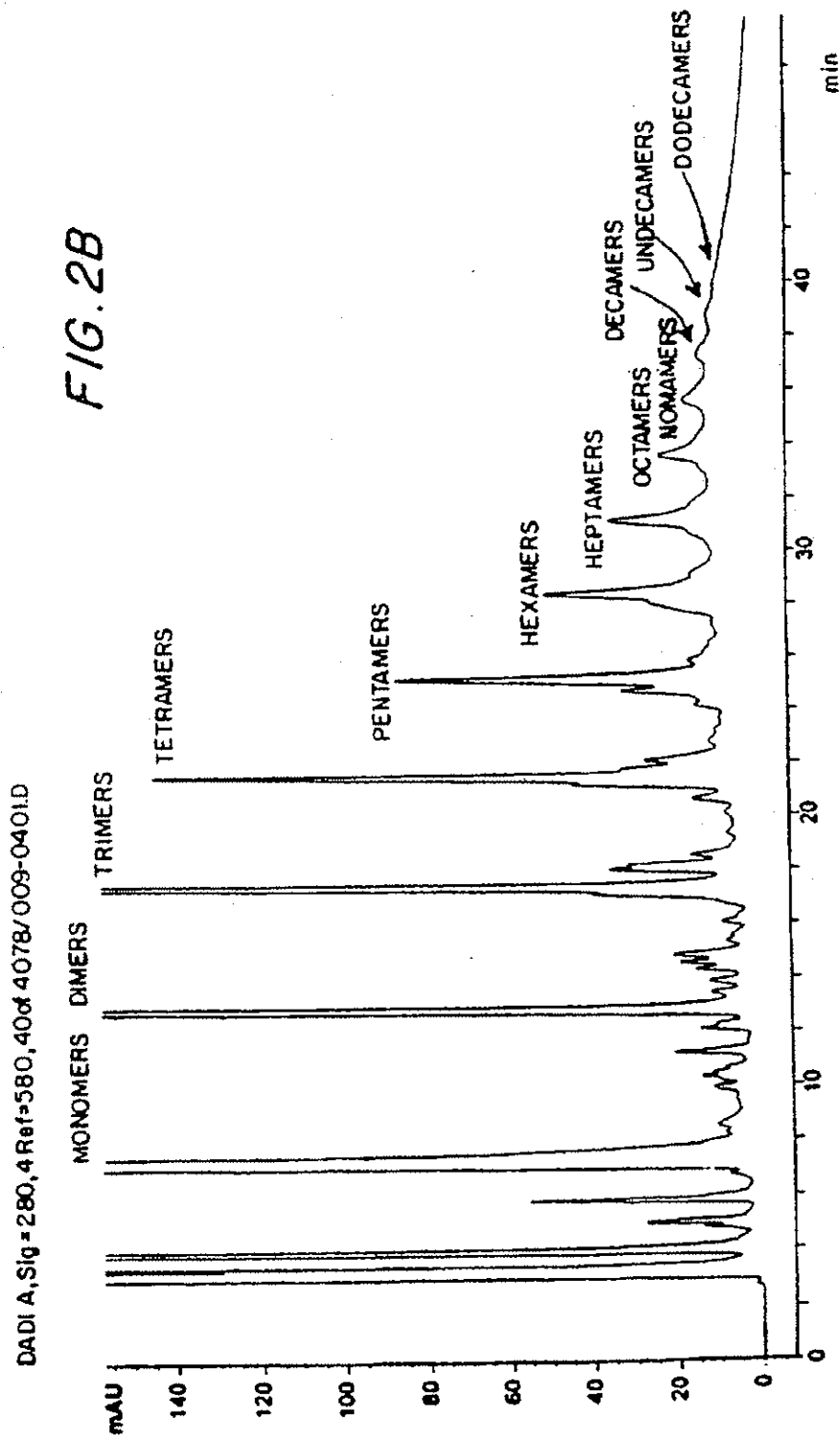
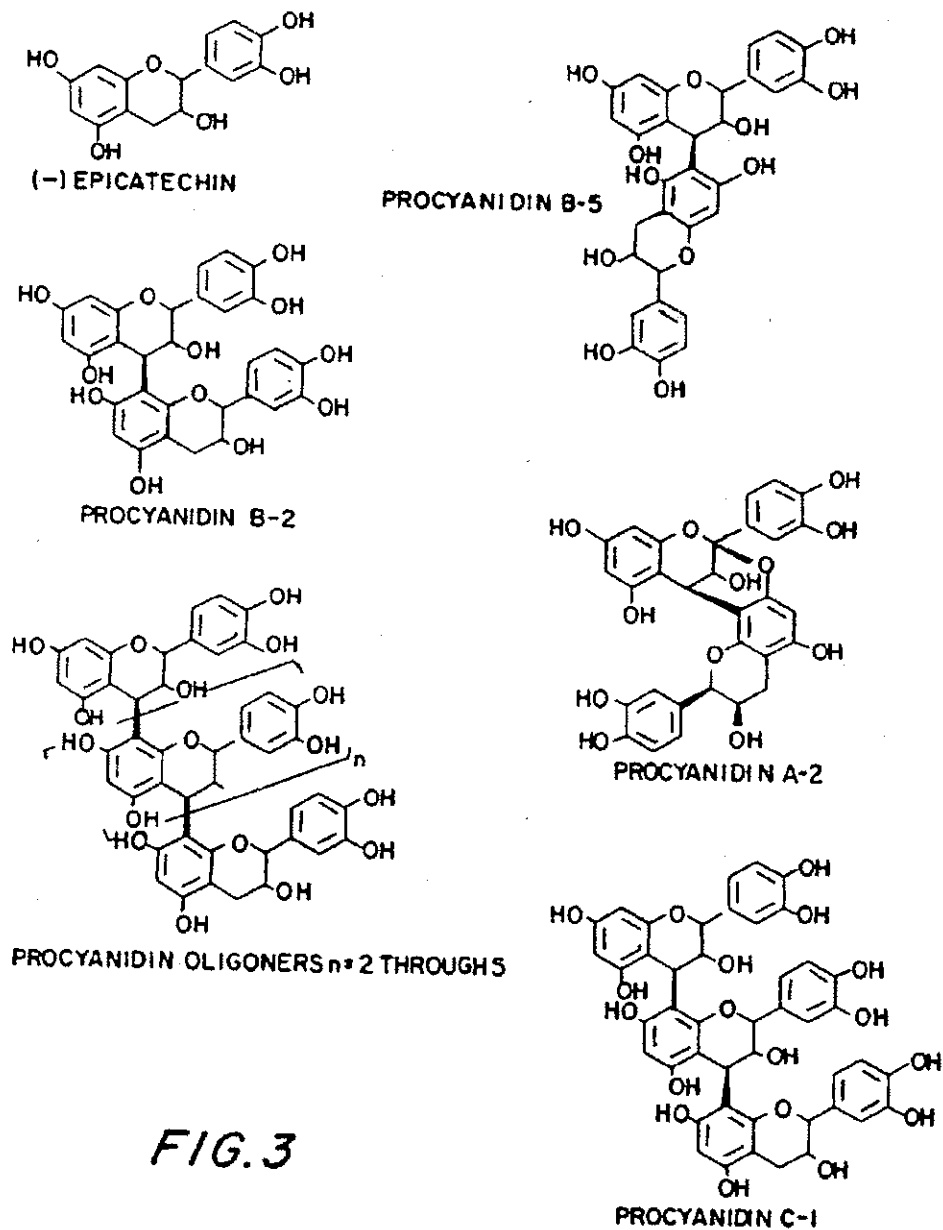


FIG. 2A





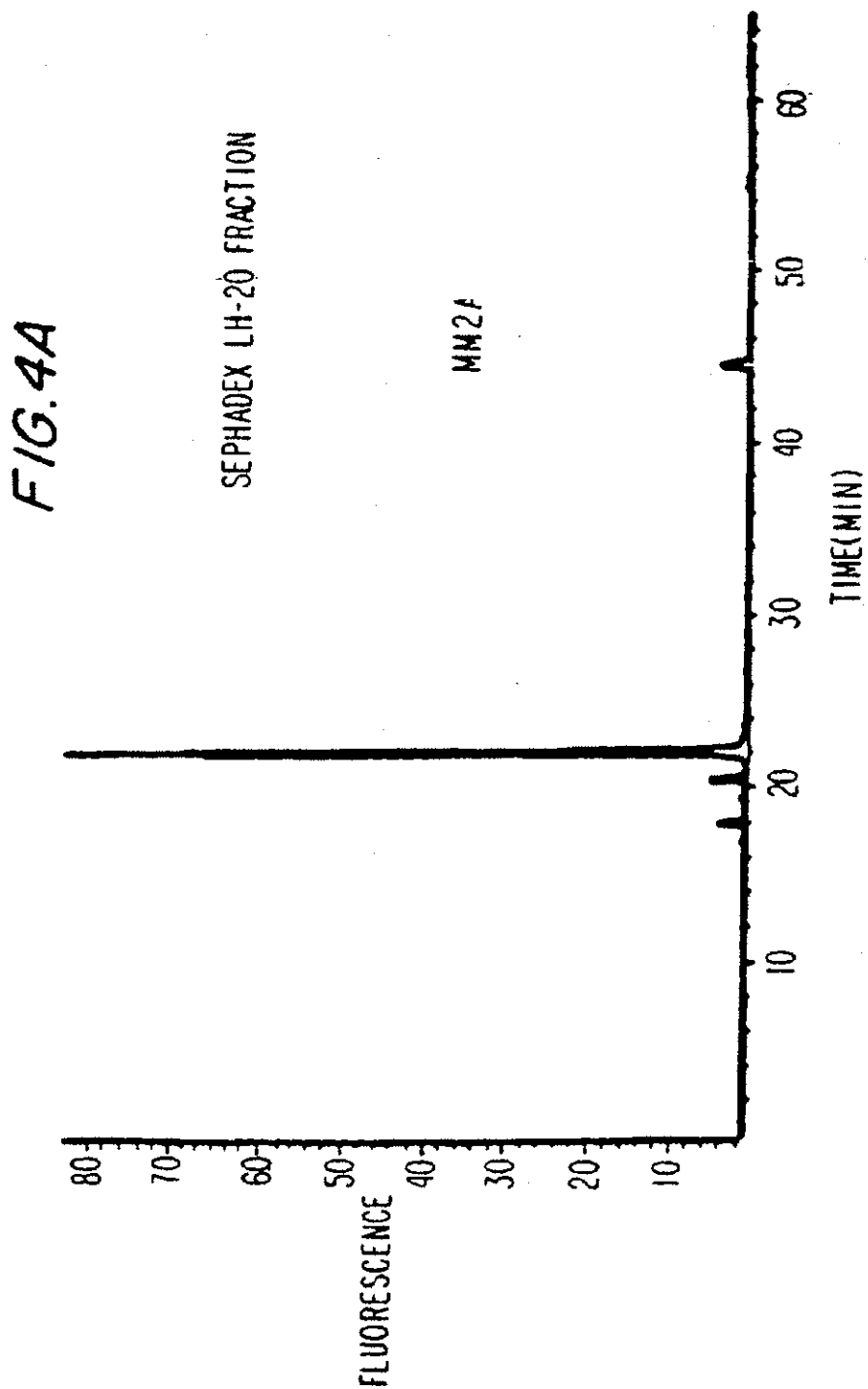


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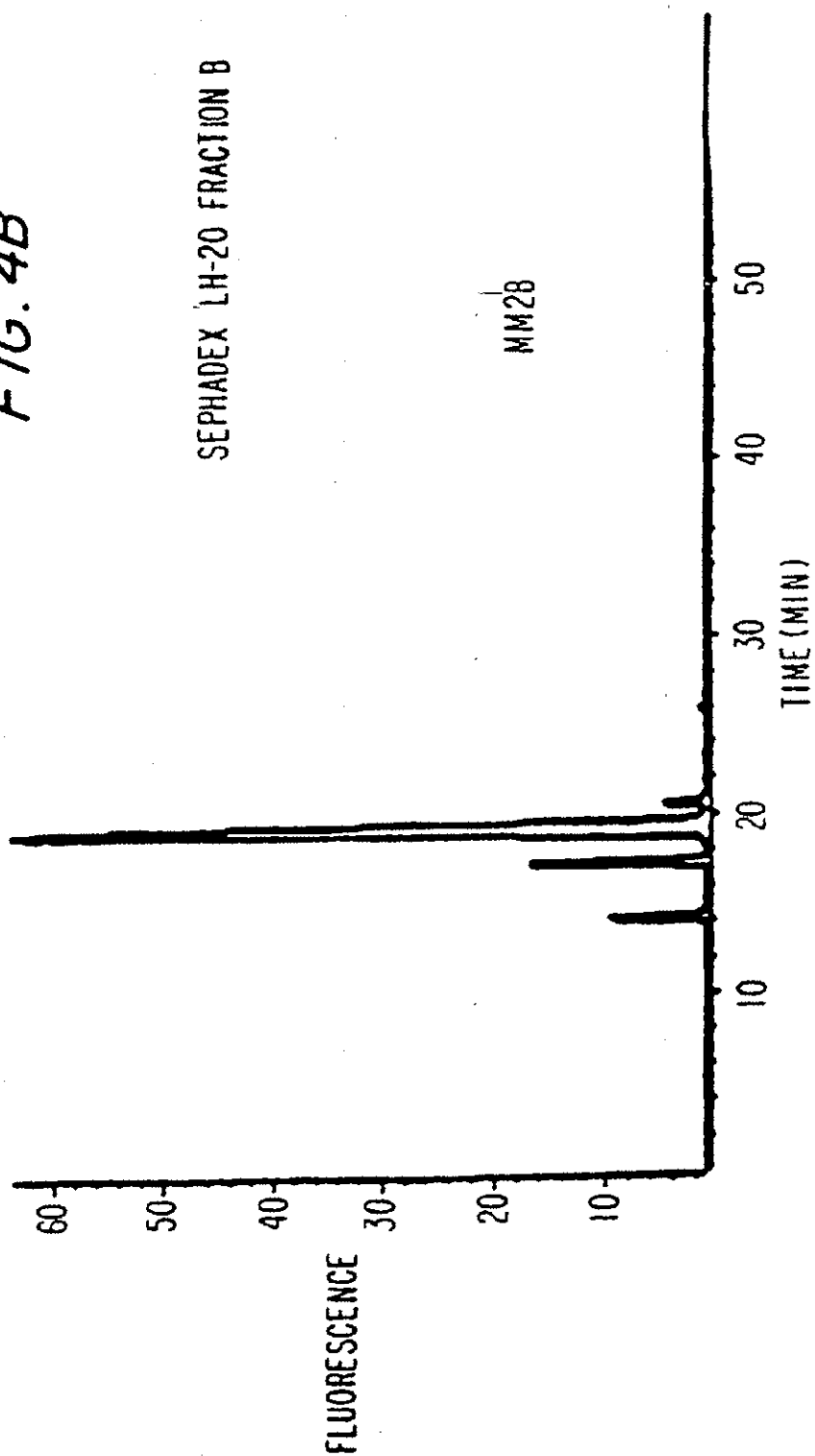
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FIG. 4B



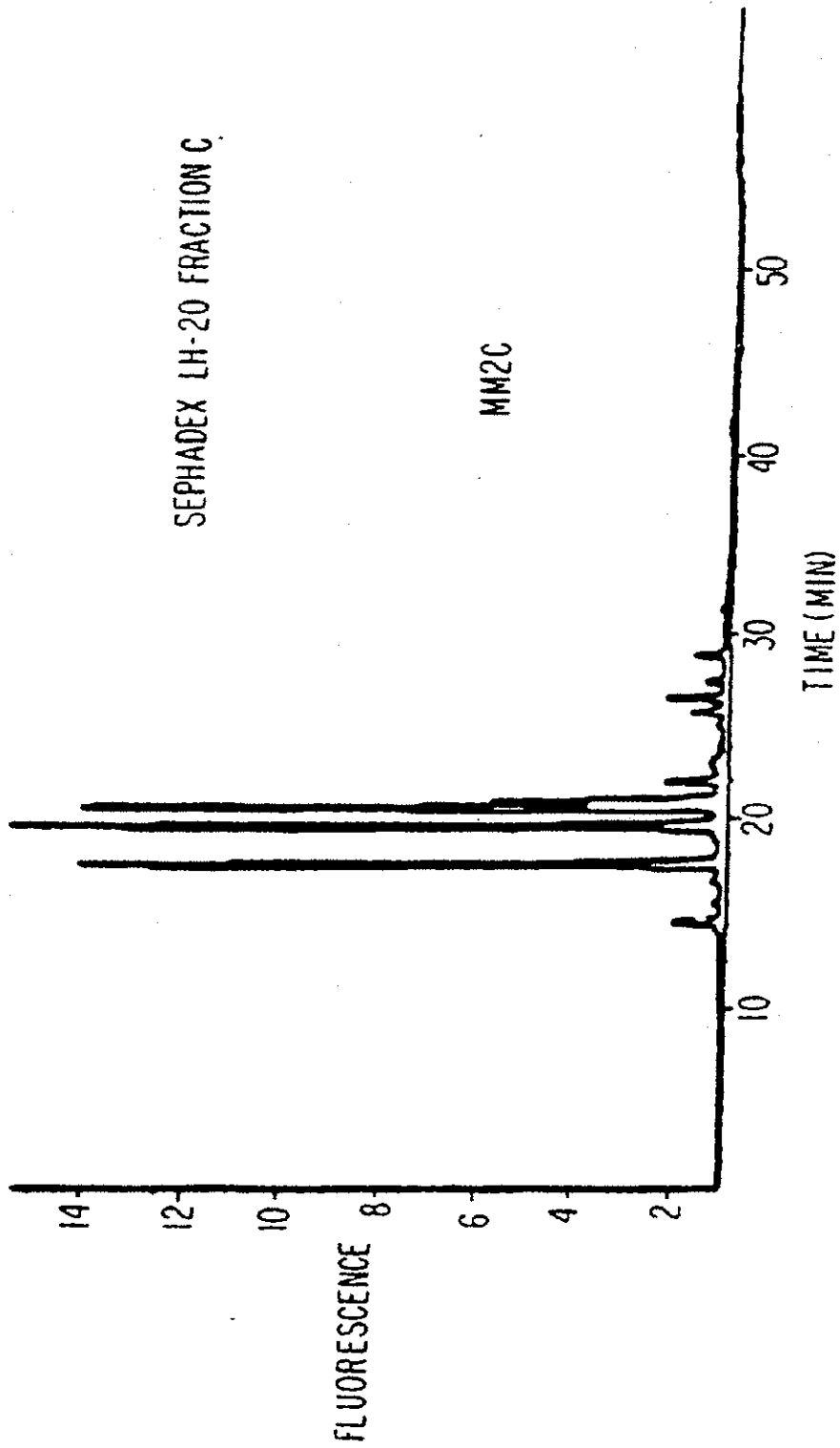
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FIG. 4C



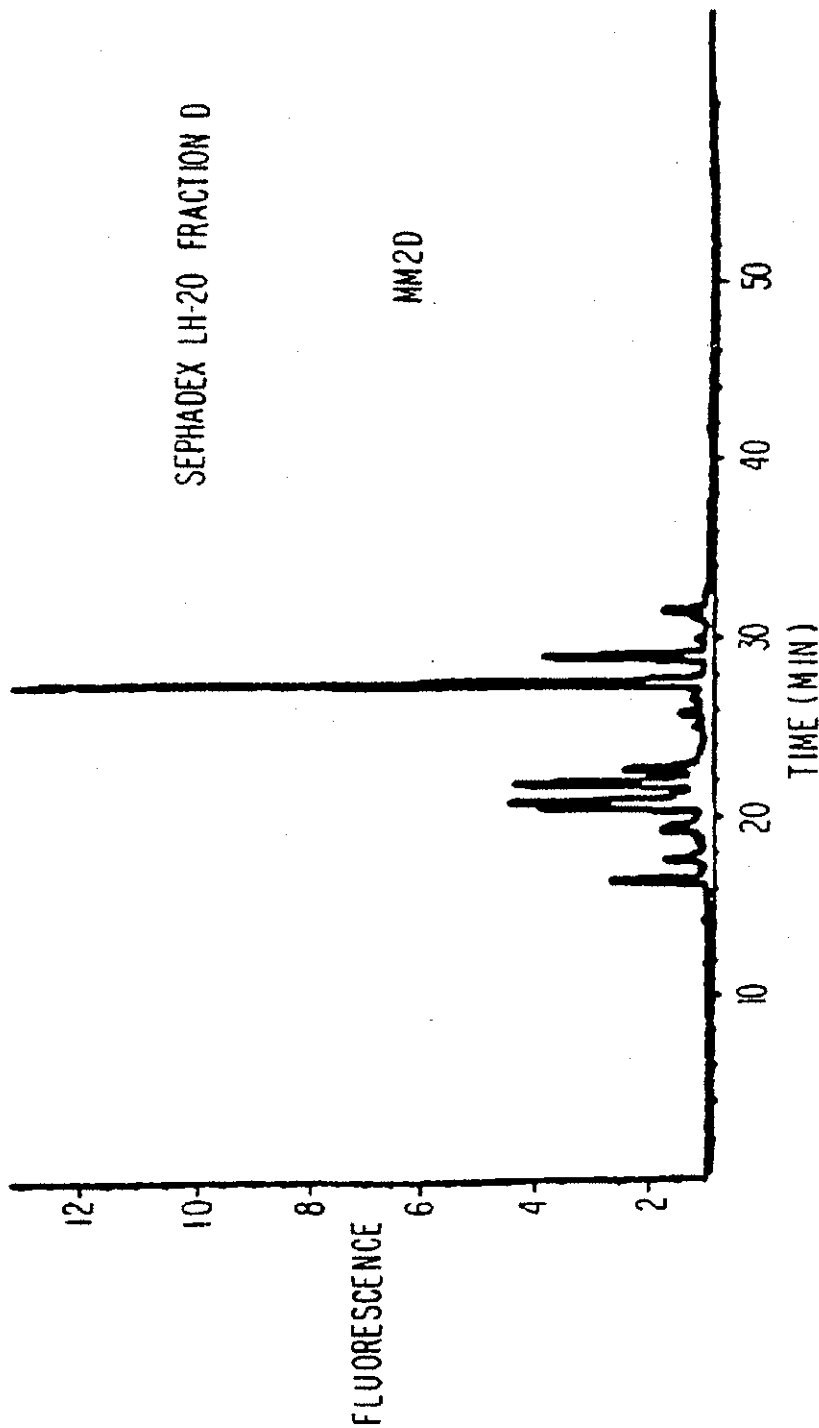
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FIG. 4D



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FIG. 4E

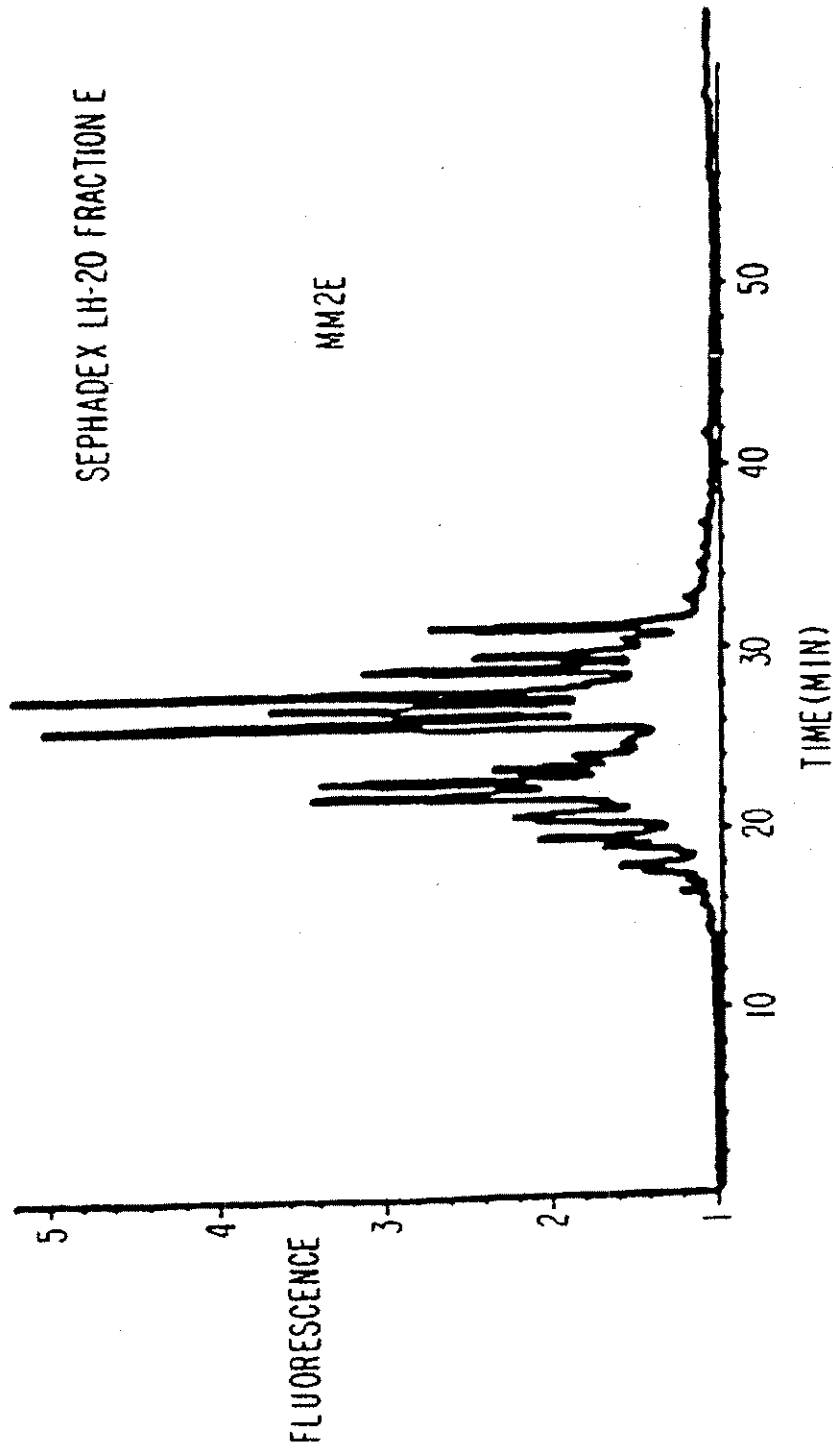
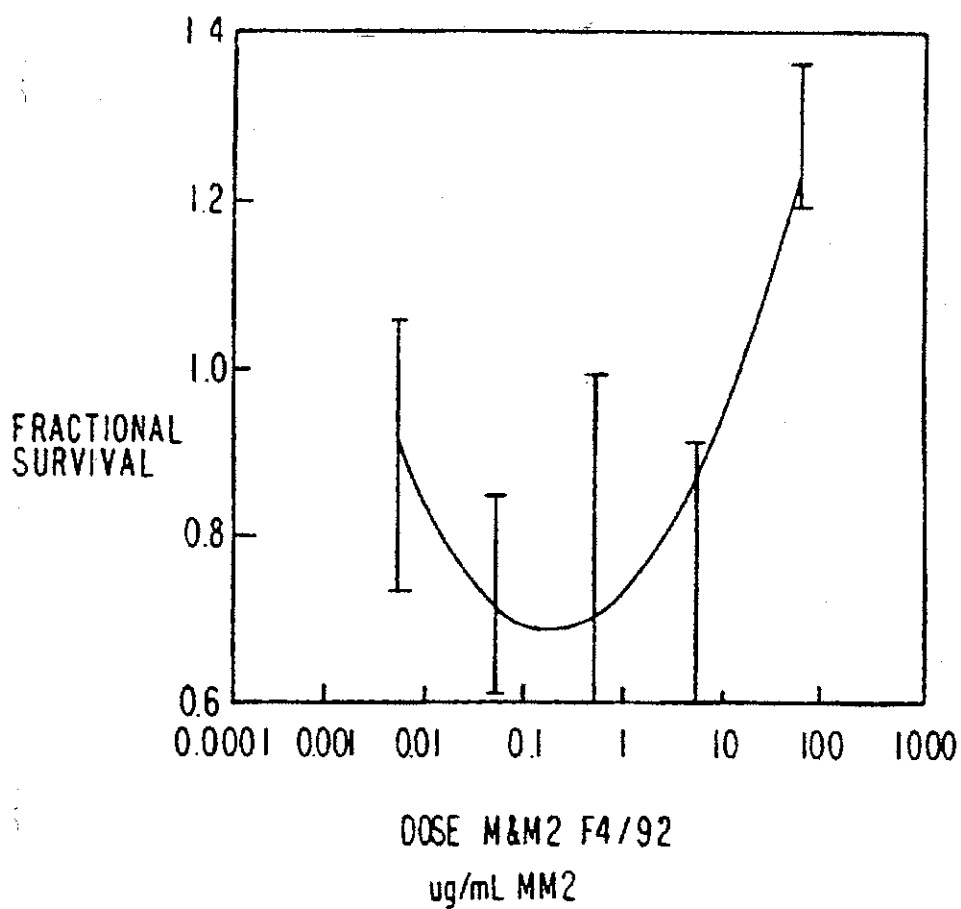


FIG. 5



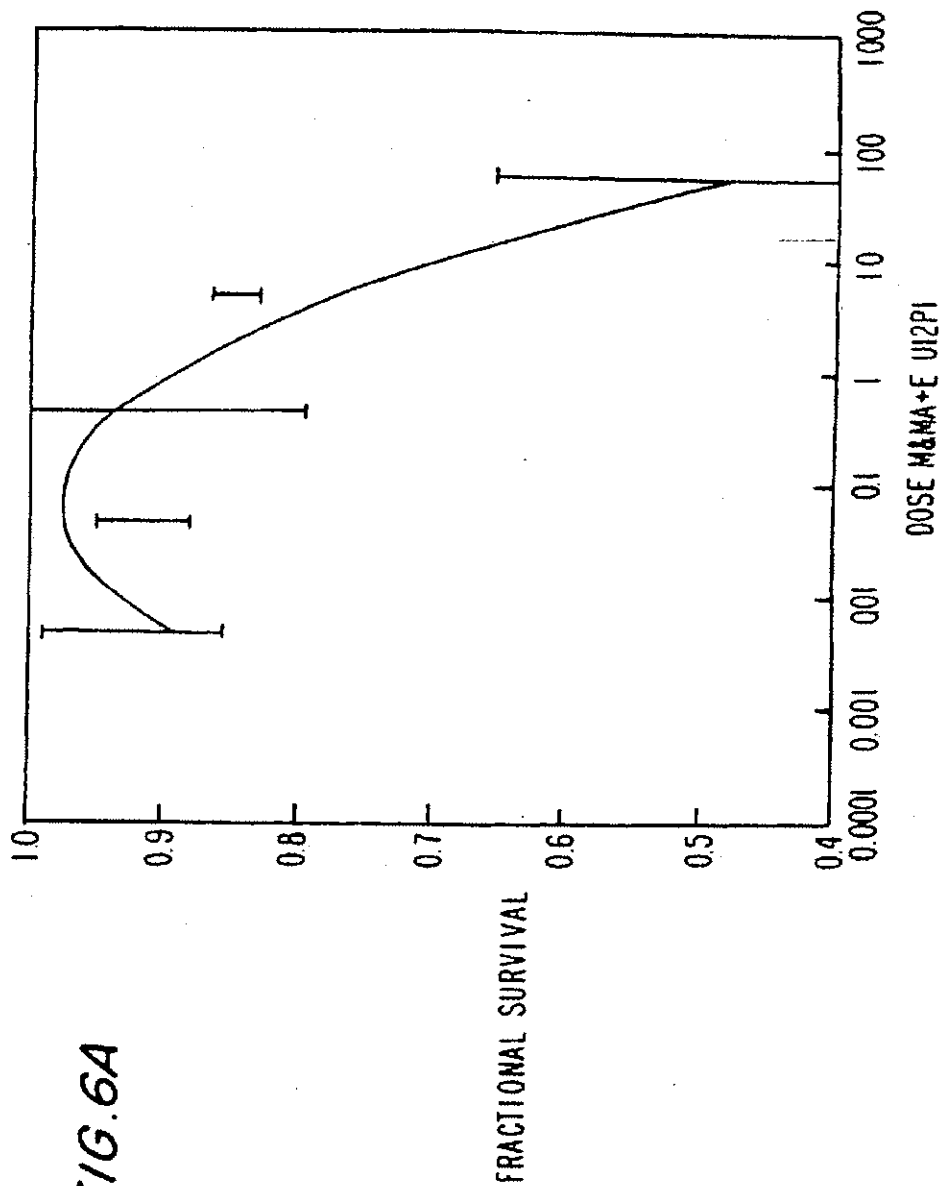


FIG. 6A

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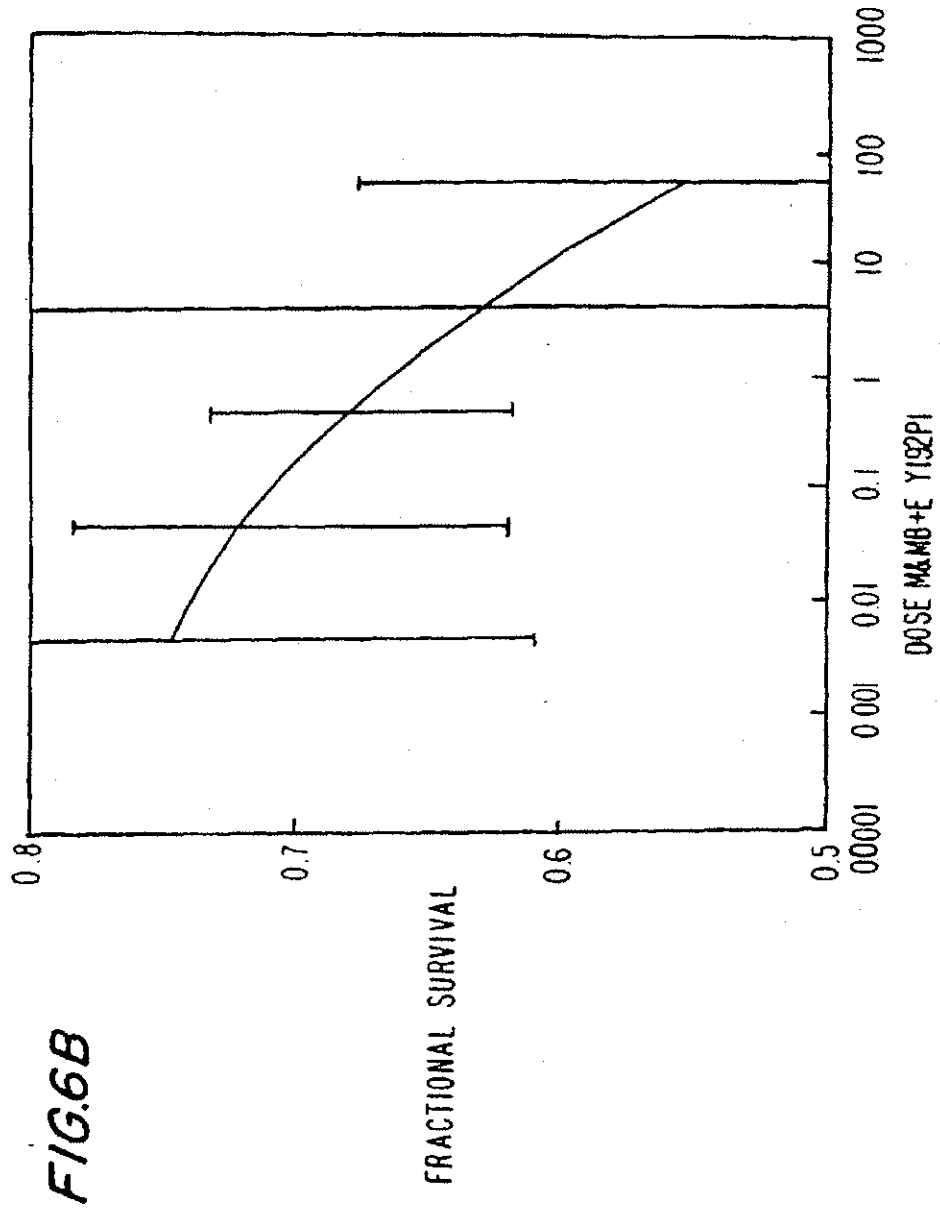


FIG.6B

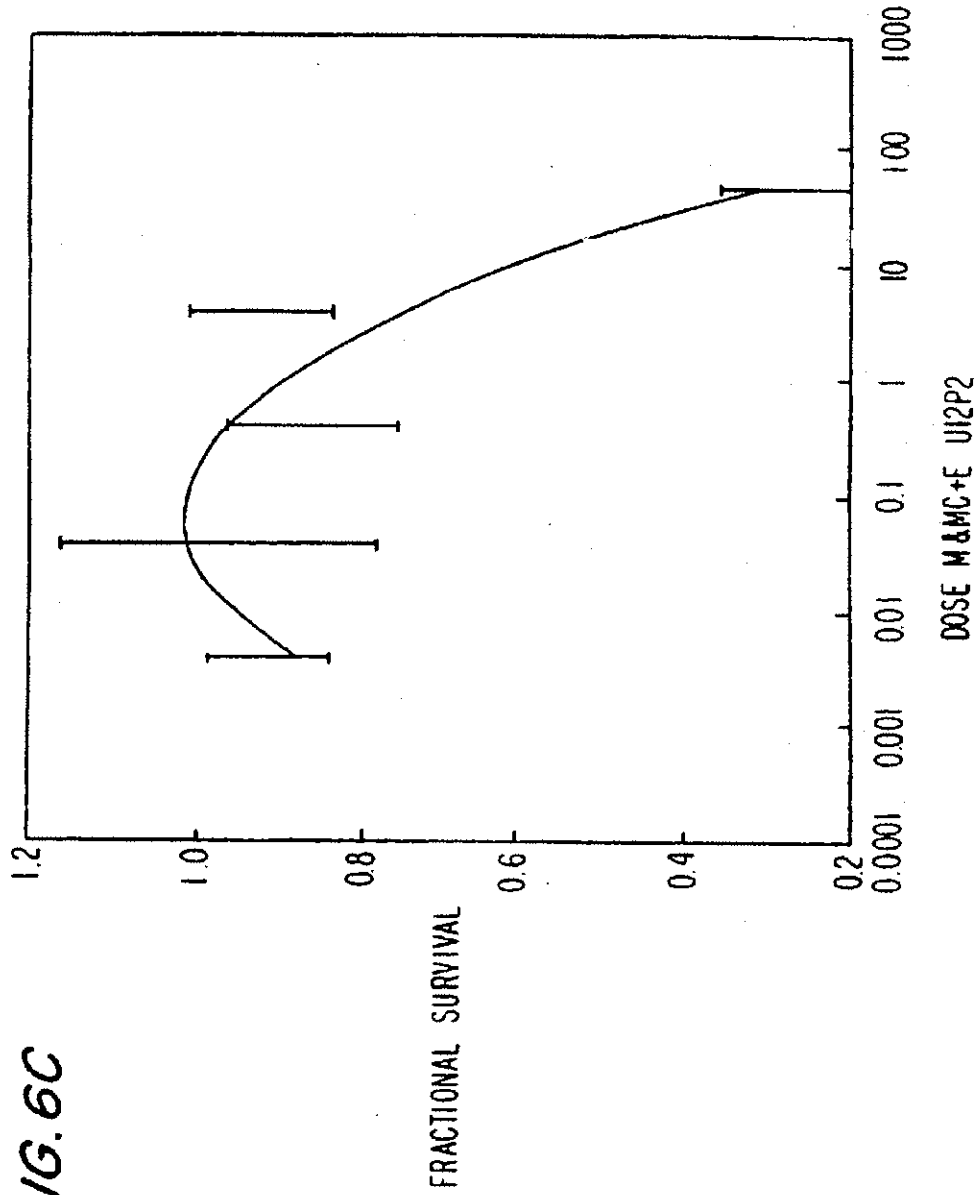


FIG. 6C

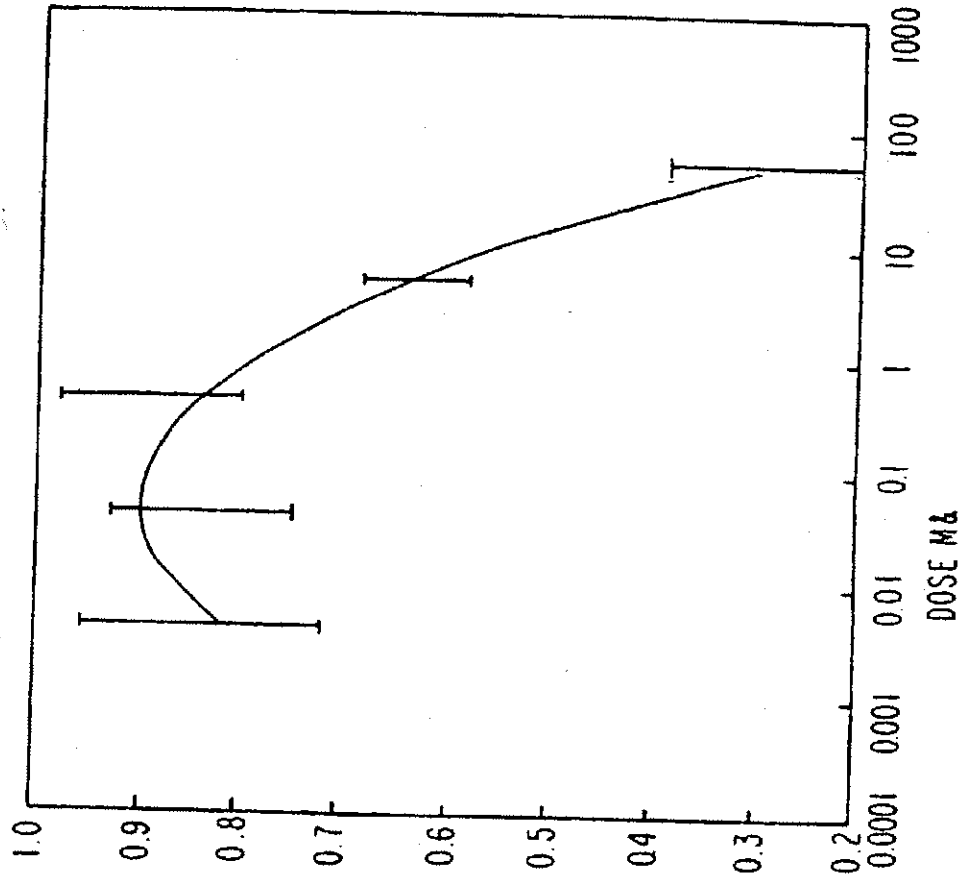


FIG. 6D

FRACTIONAL SURVIVAL

FIG. 7A

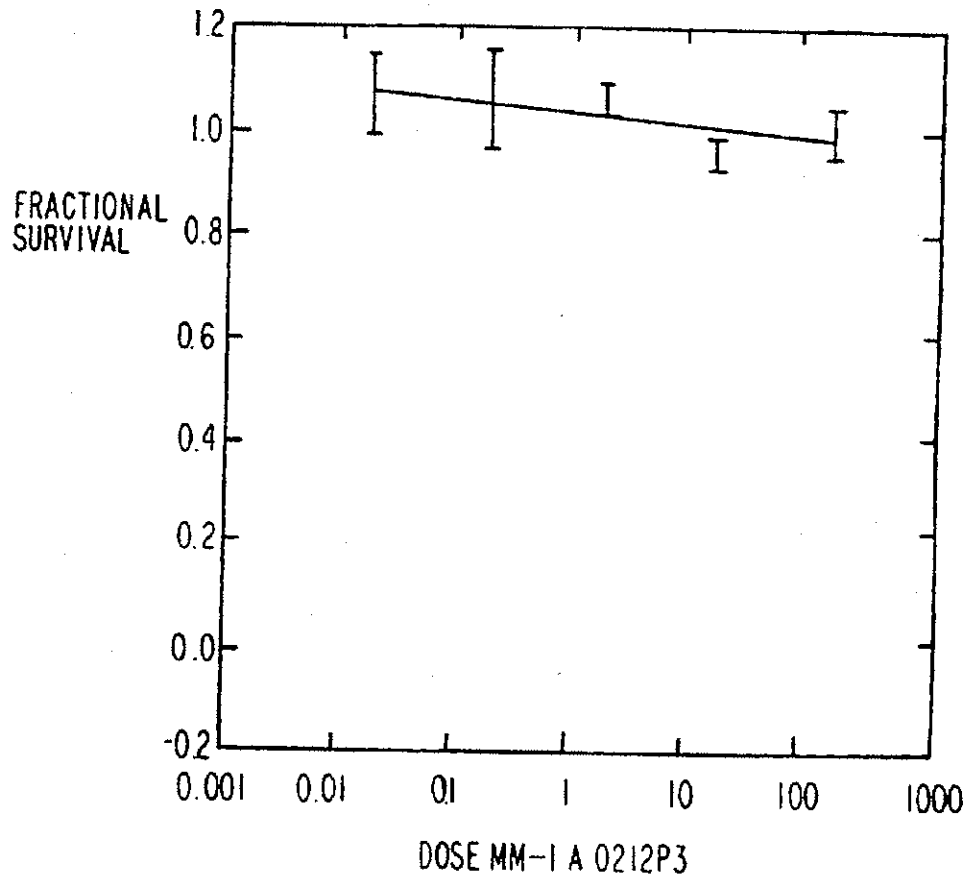


FIG. 7B

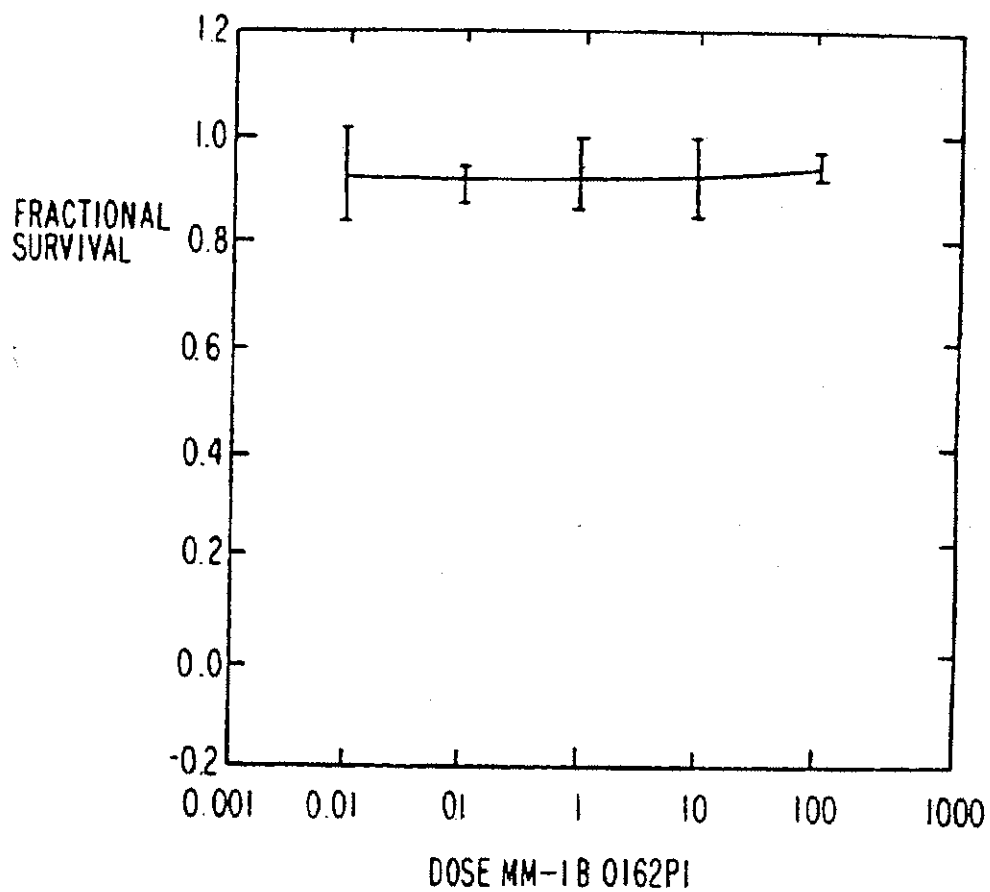


FIG. 7C

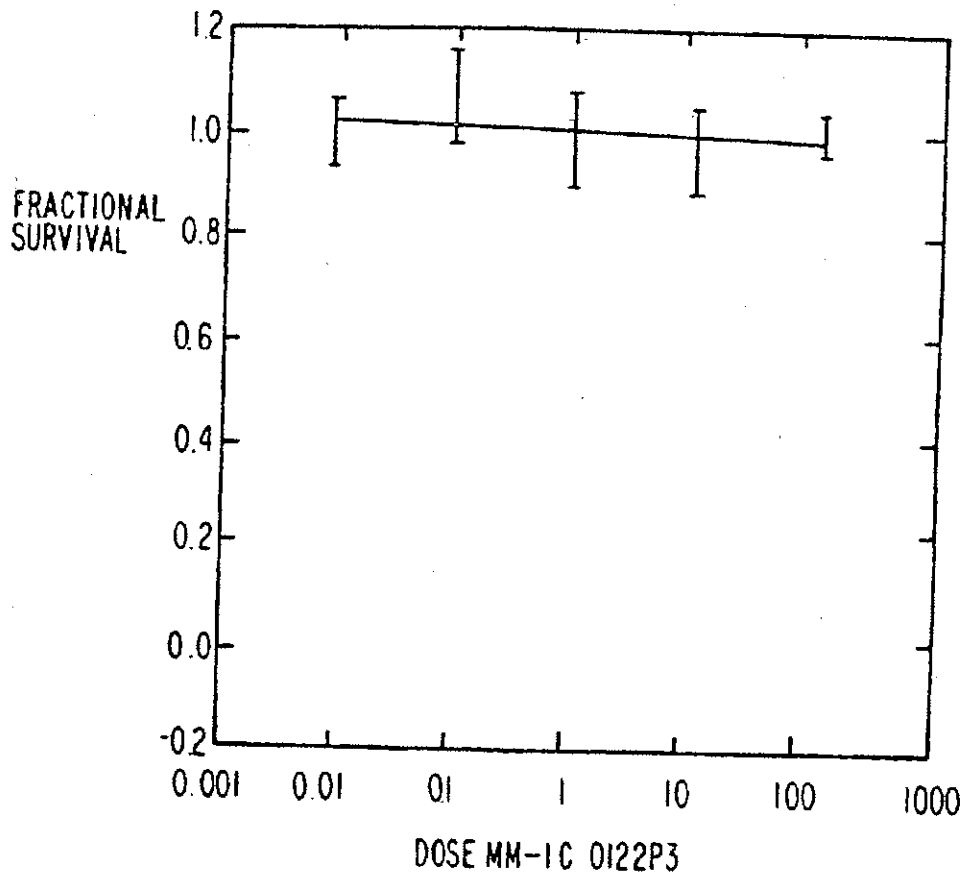
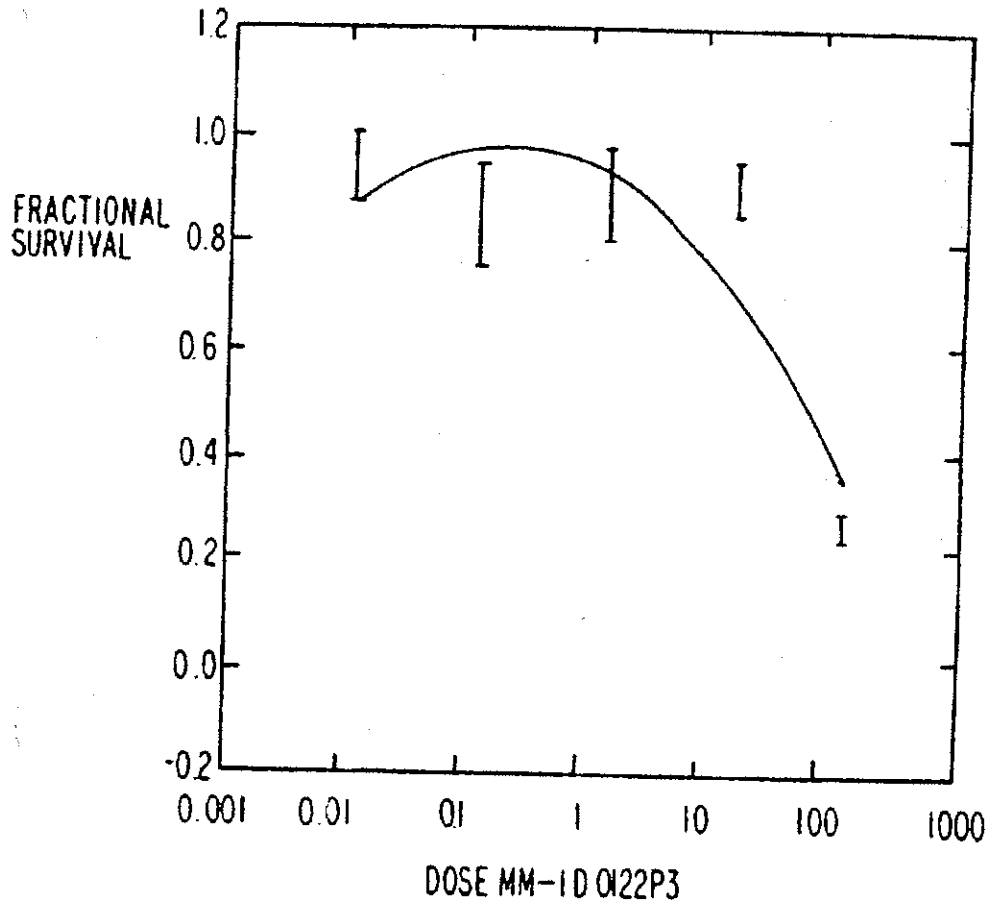


FIG. 7D



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FIG. 7E

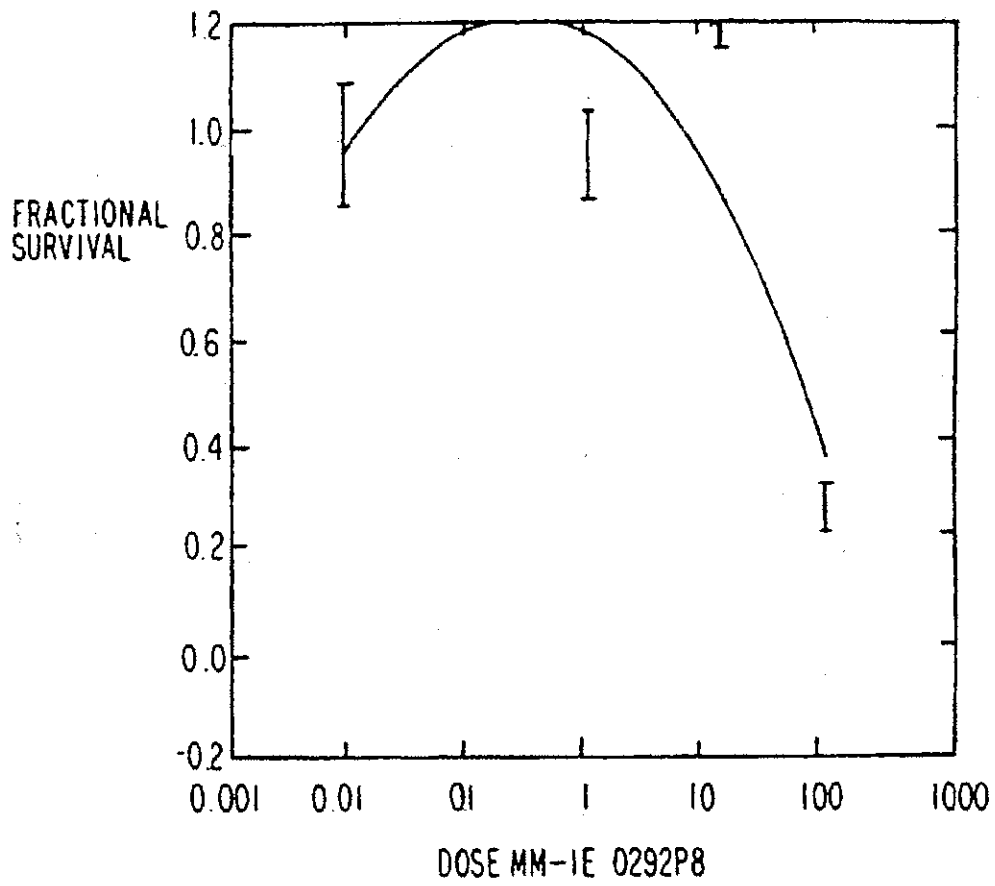


FIG. 7F

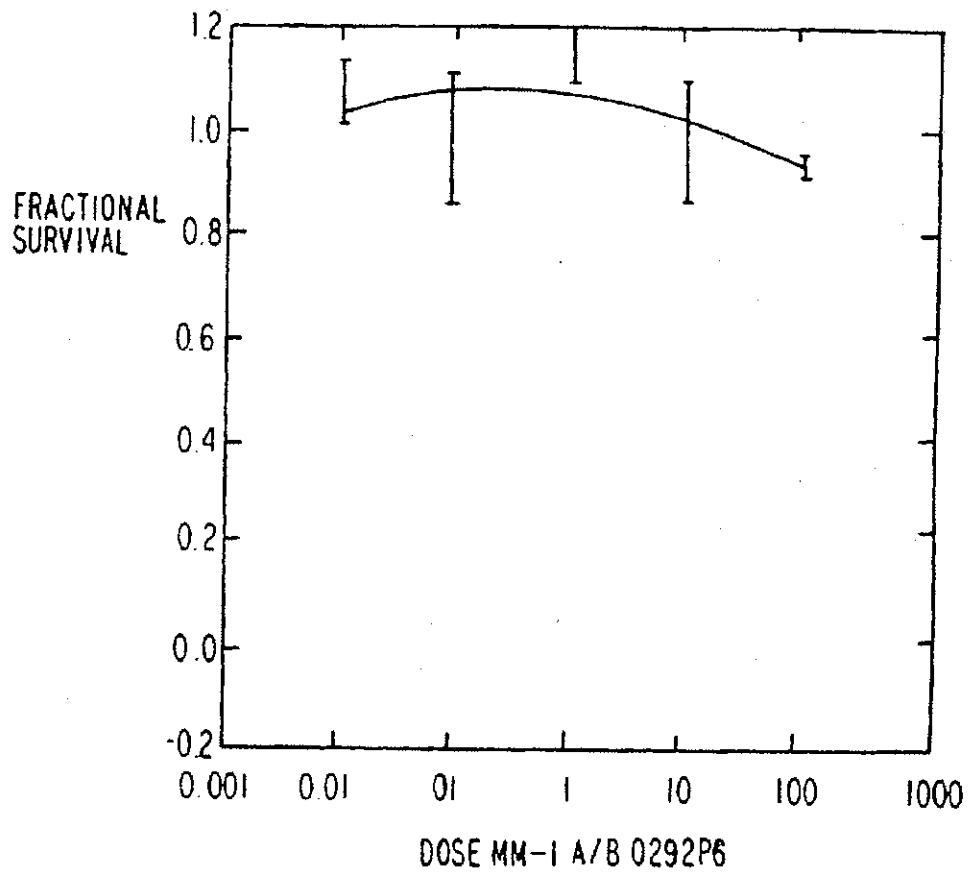
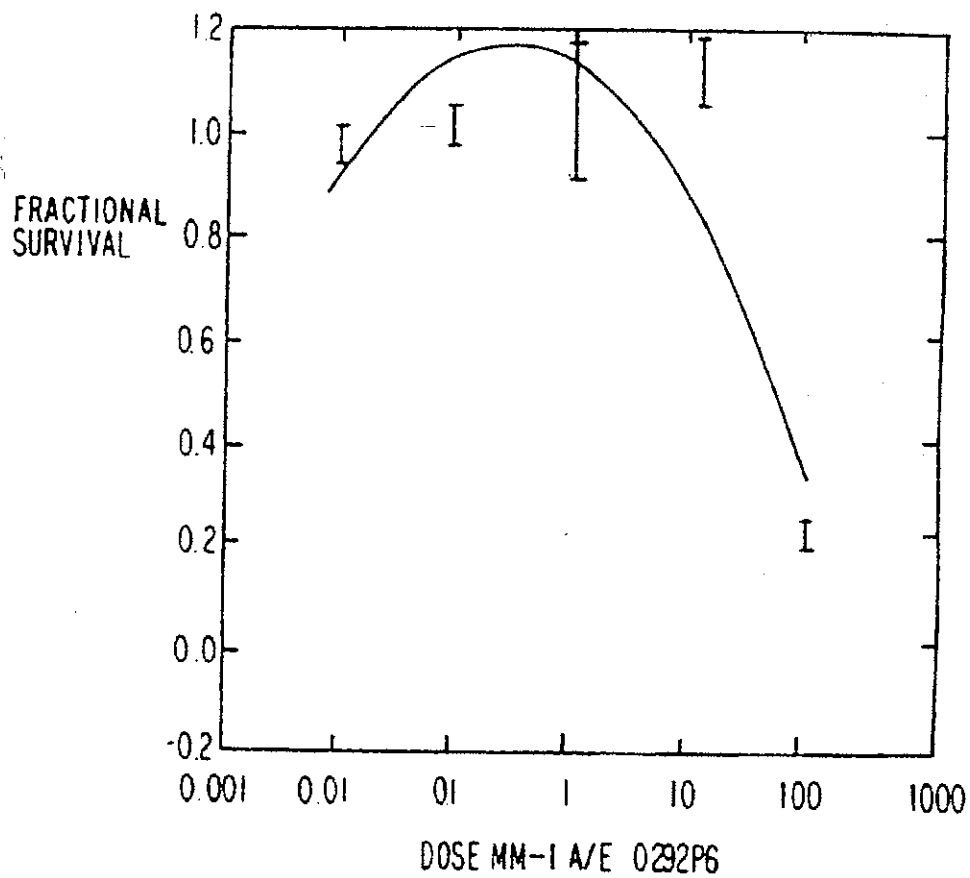


FIG. 7G



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FIG. 7H

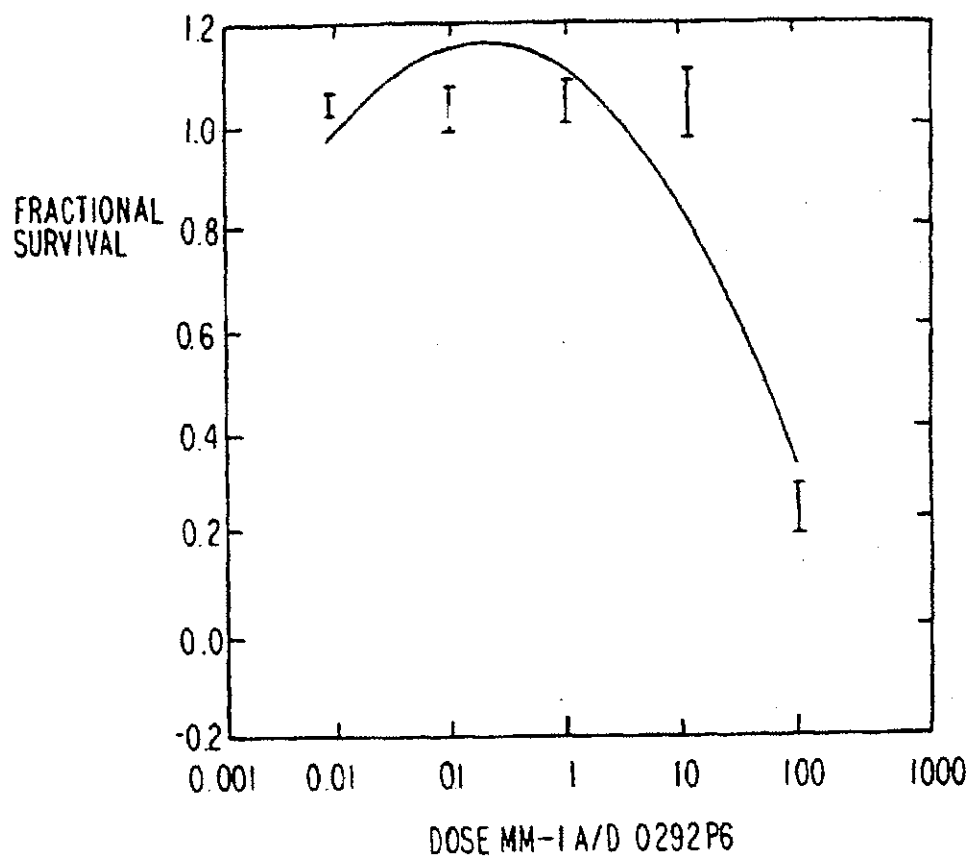


FIG. 8A

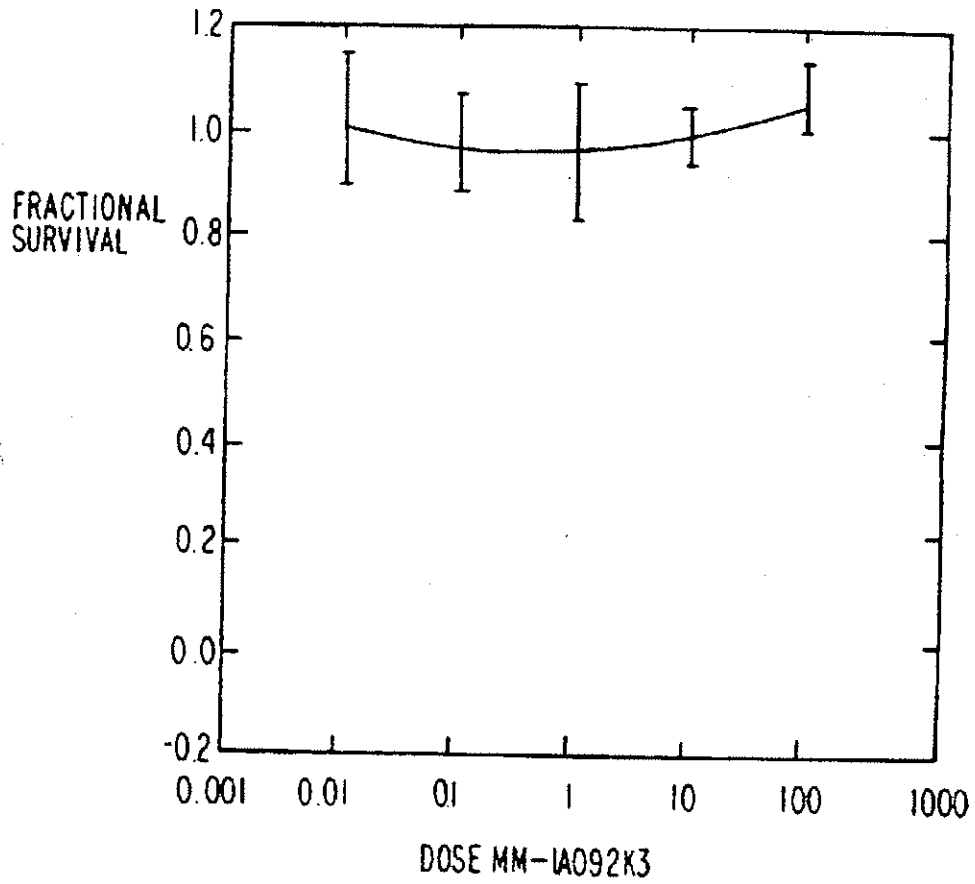
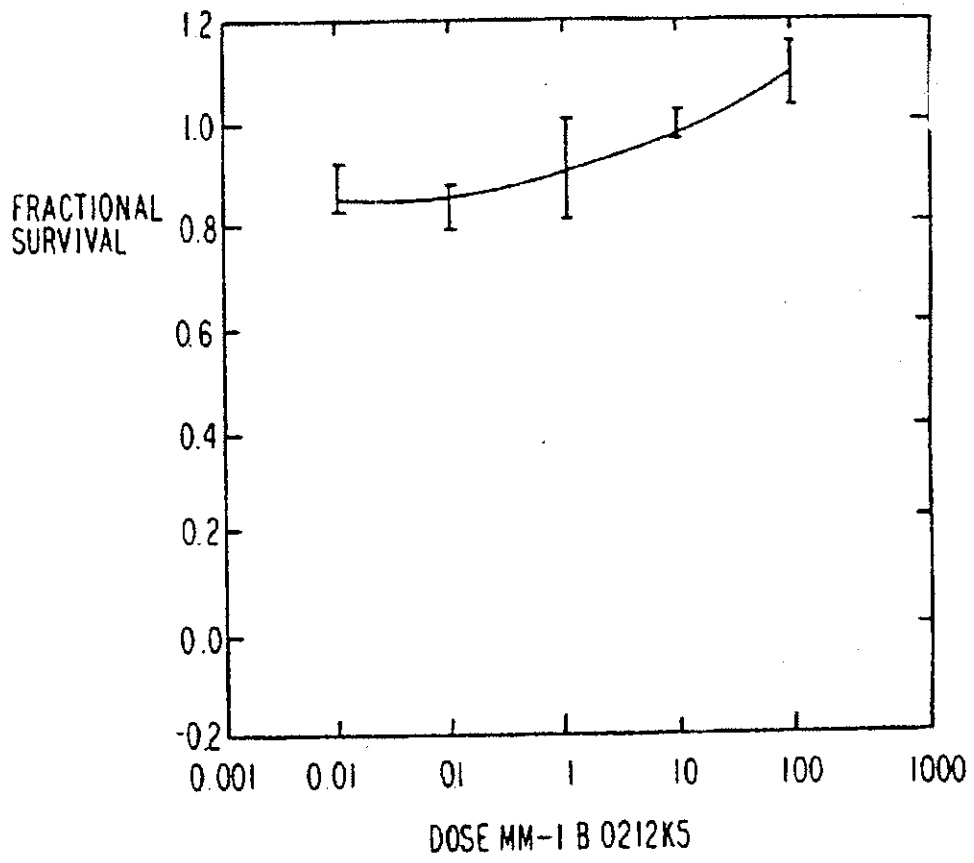


FIG. 8B



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FIG. 8C

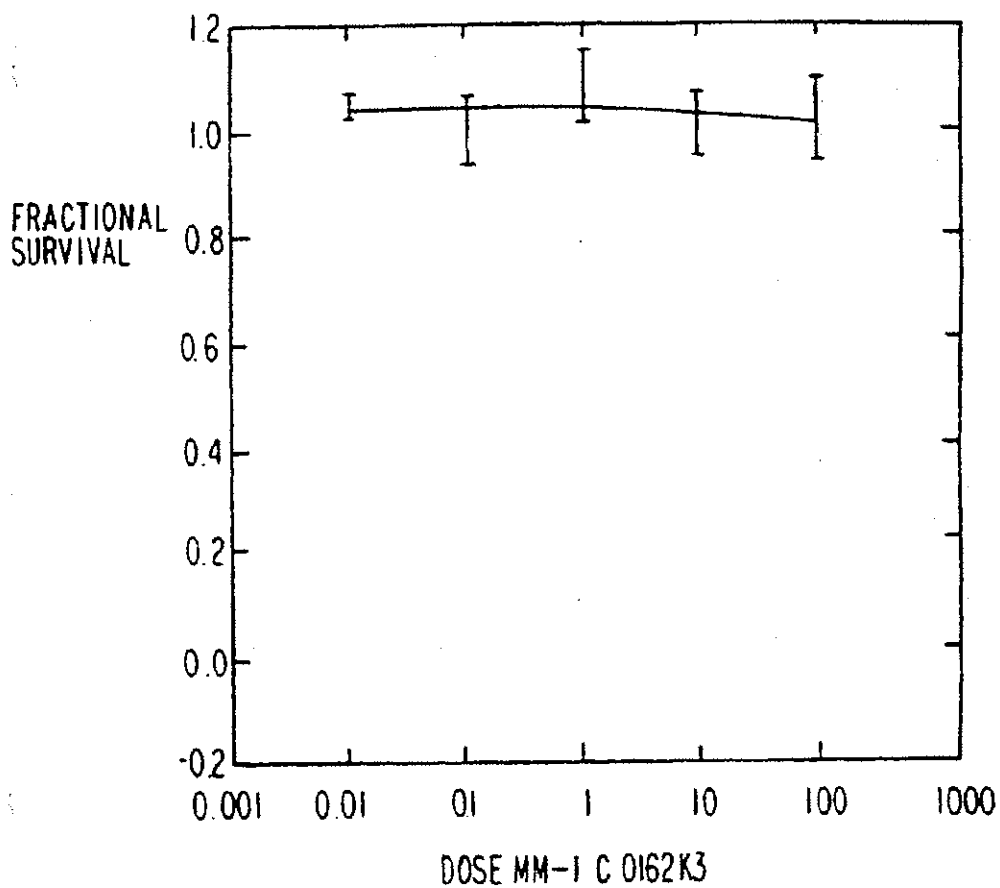
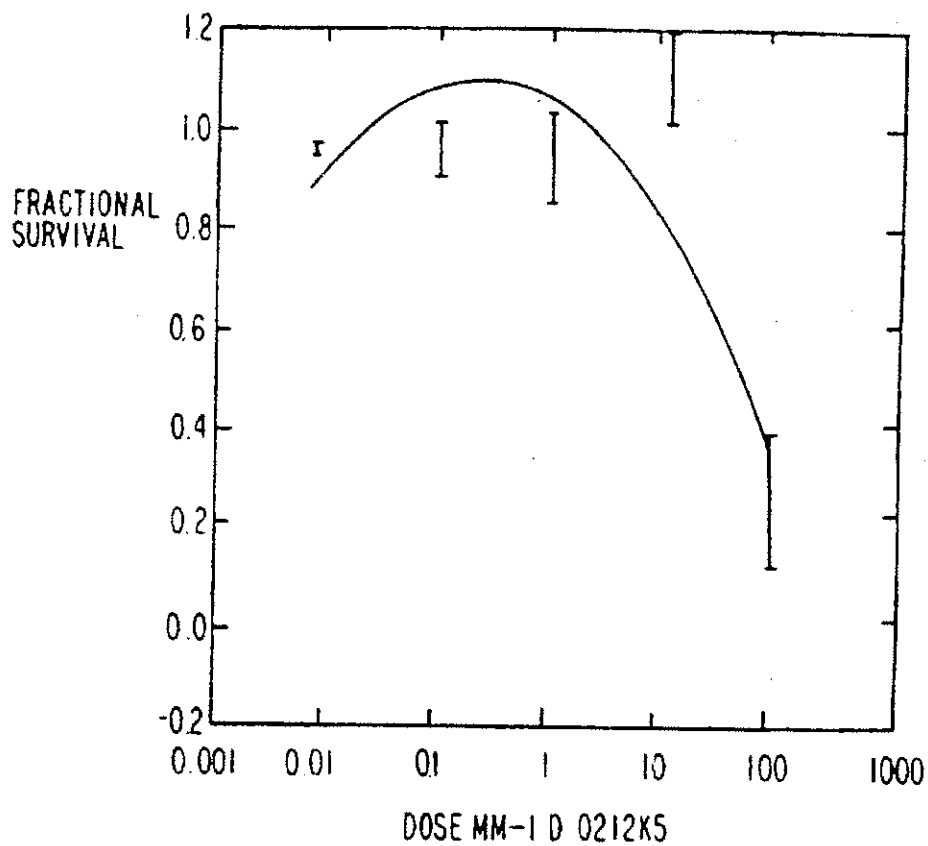


FIG. 8D



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FIG. 8E

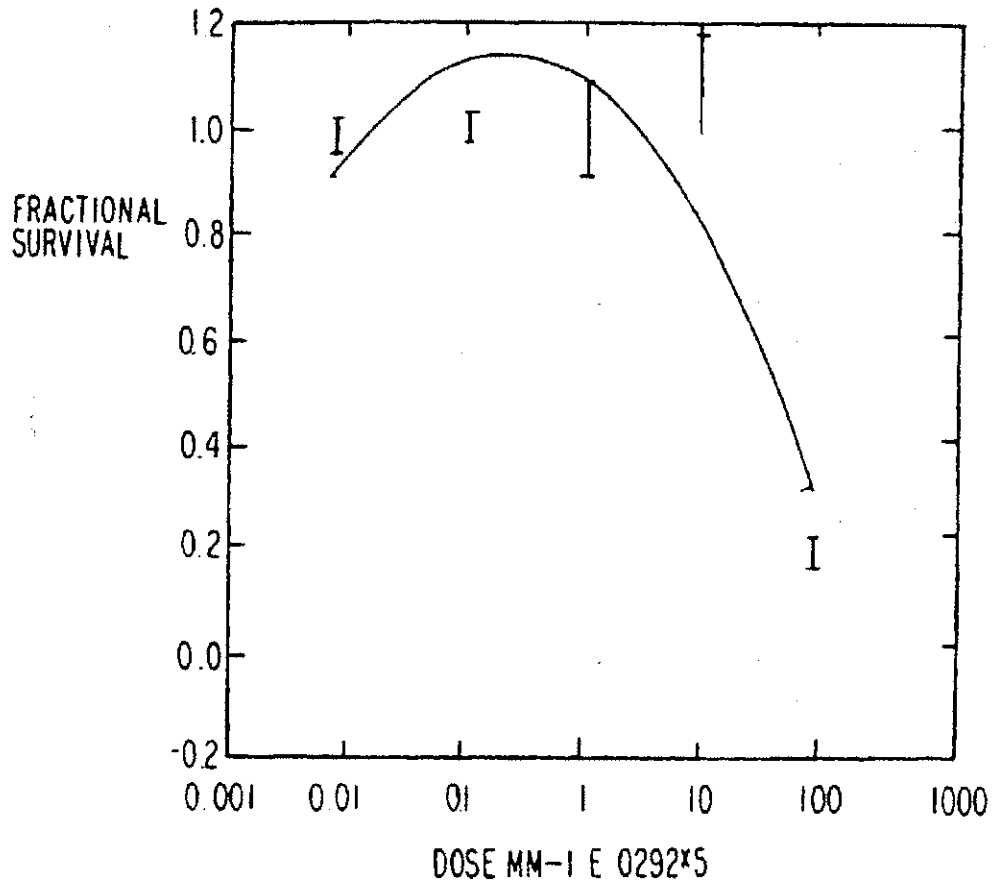


FIG. 8F

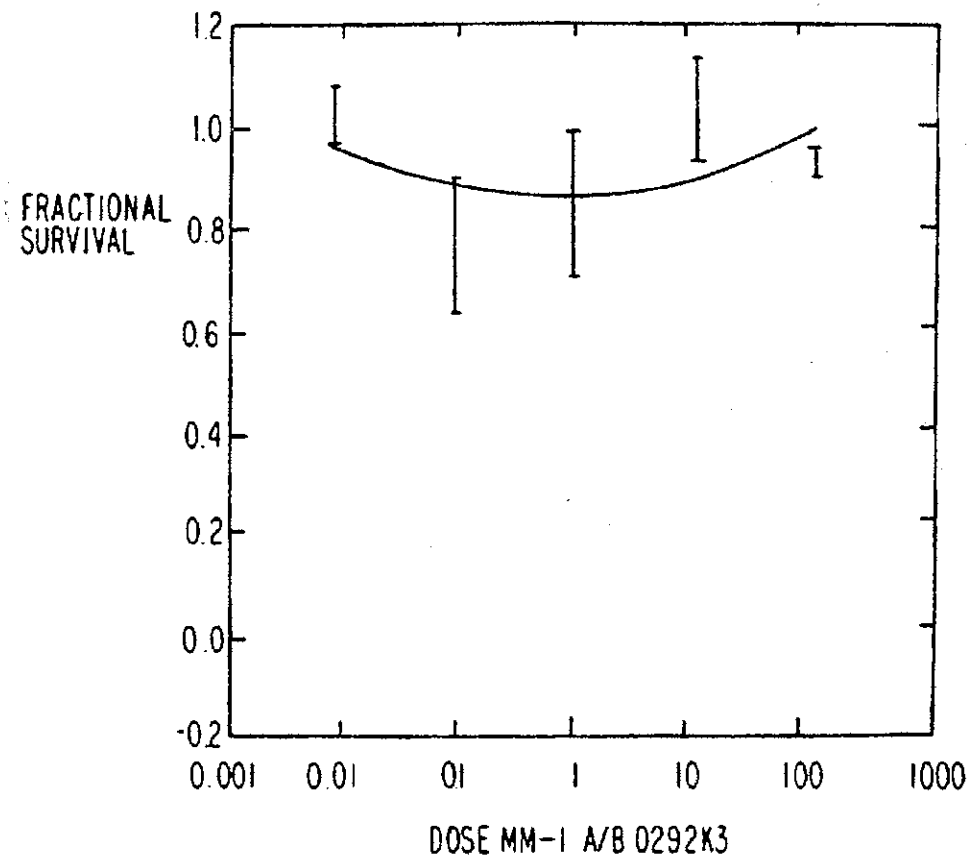


FIG. 8G

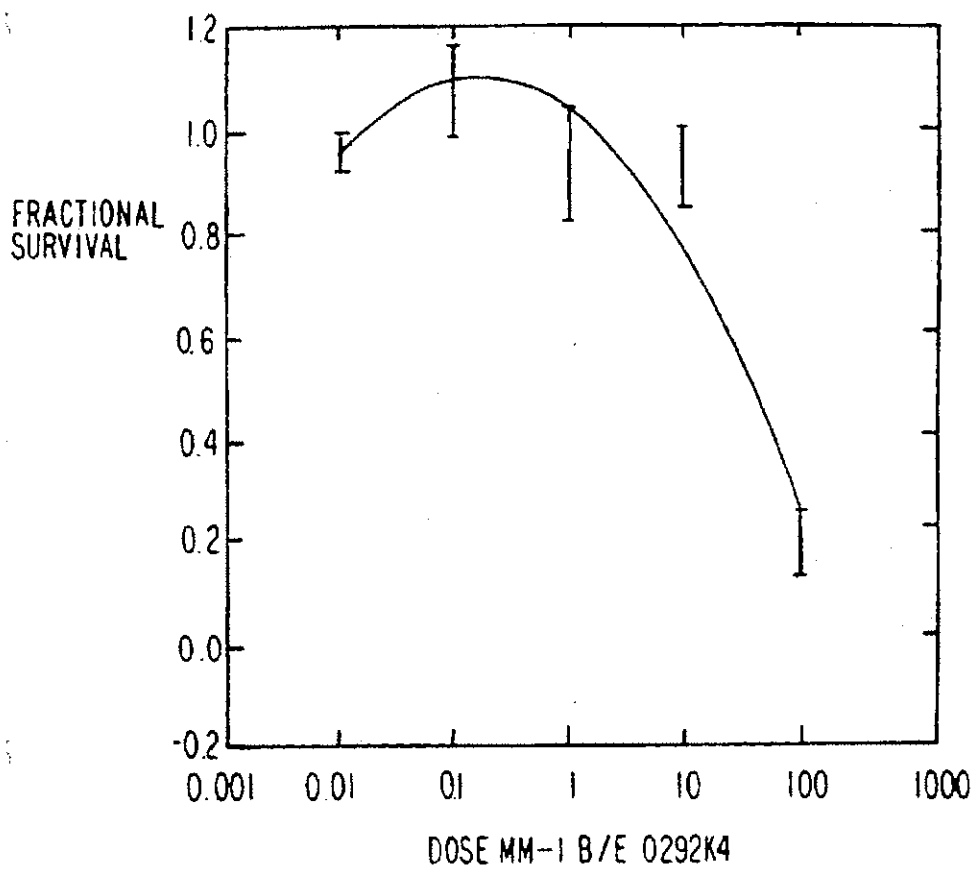
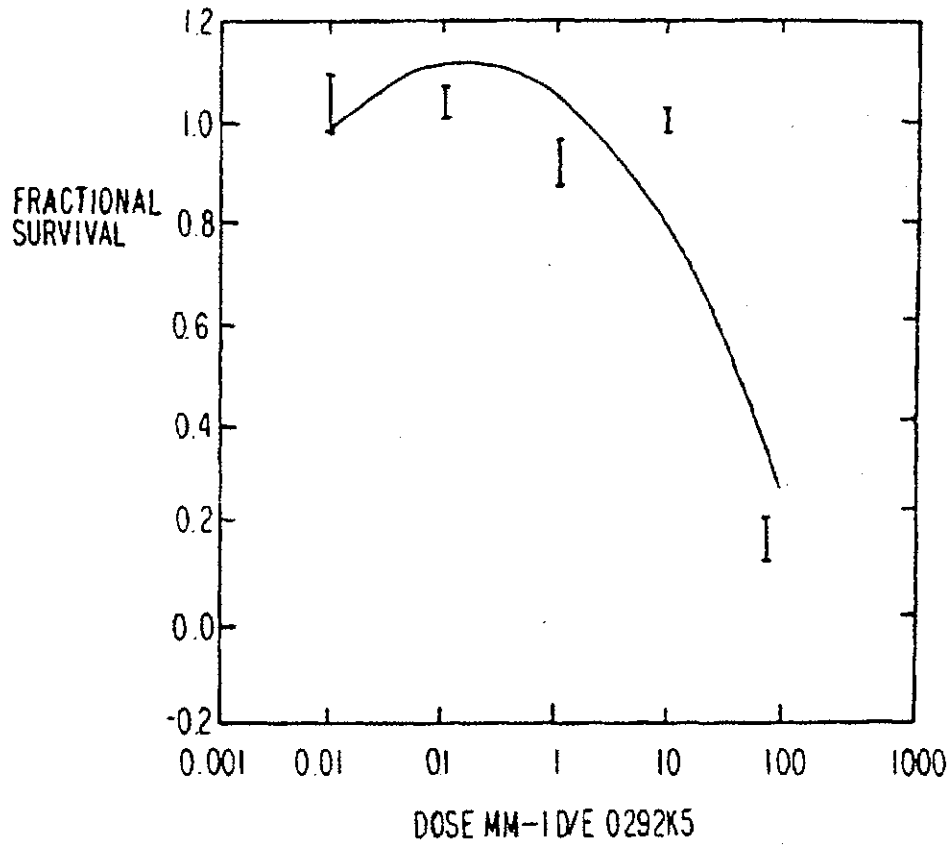


FIG. 8H



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FIG. 9A

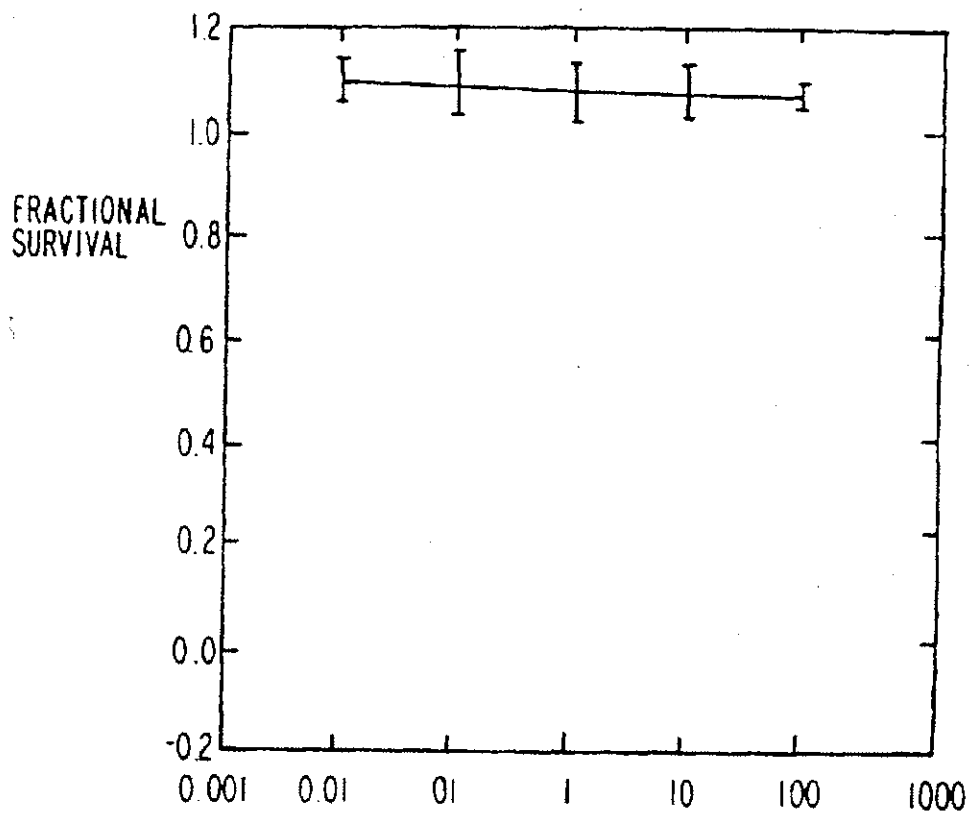


FIG. 9B

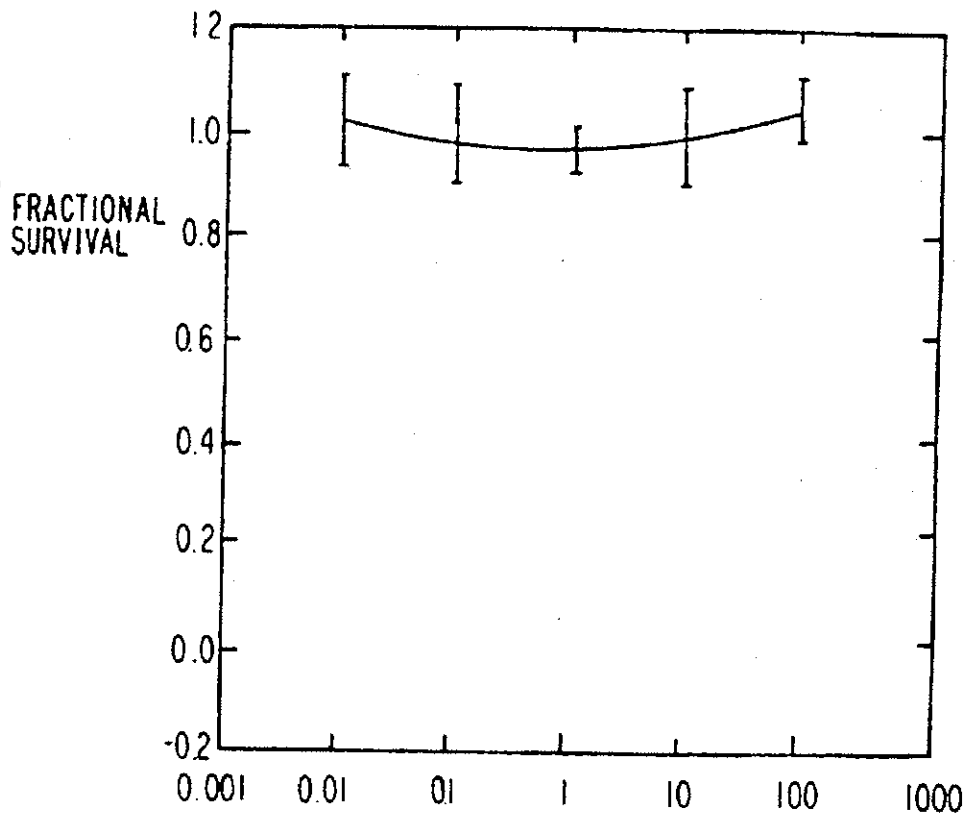


FIG. 9C

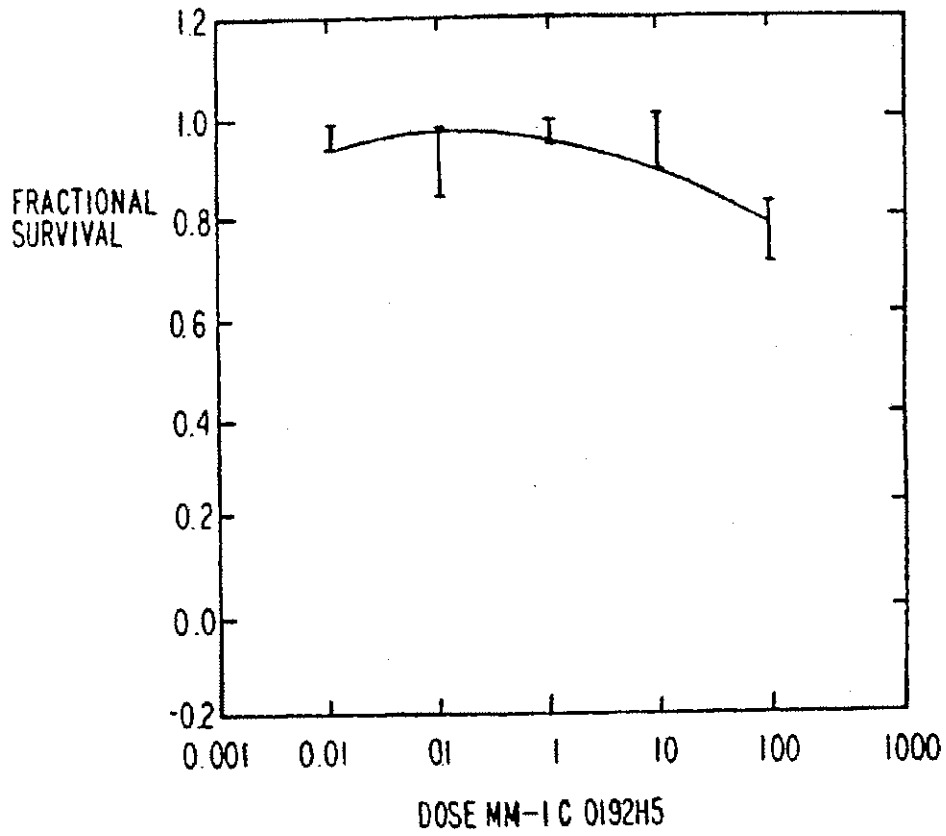


FIG. 9D

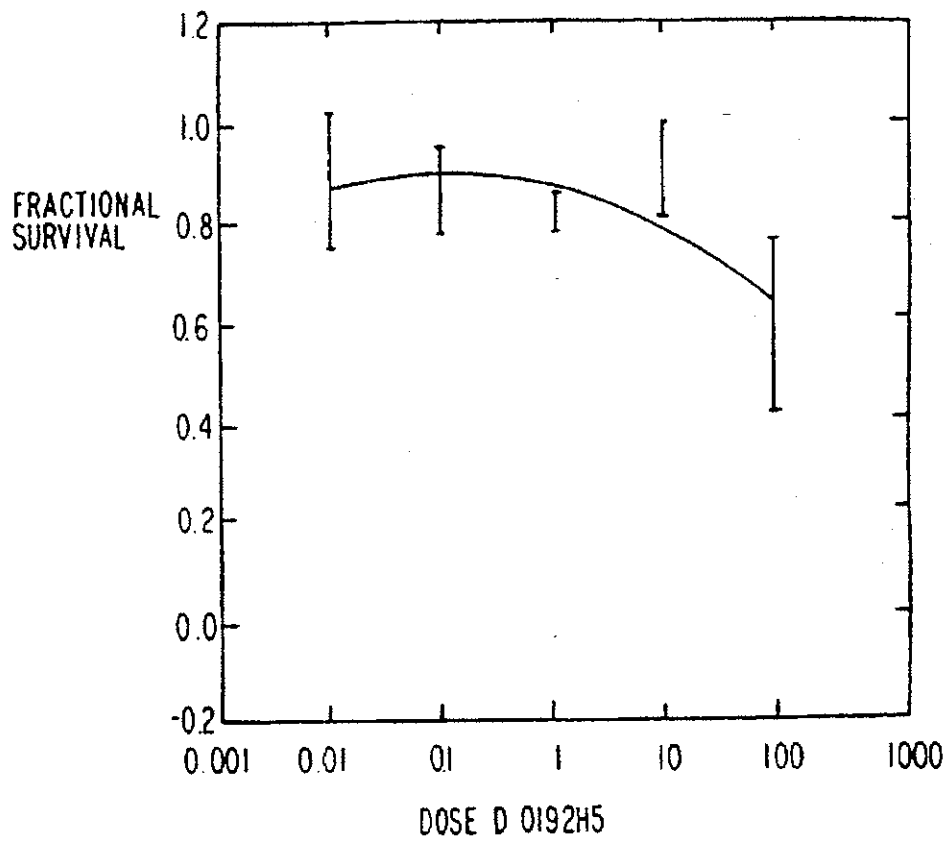


FIG. 9E

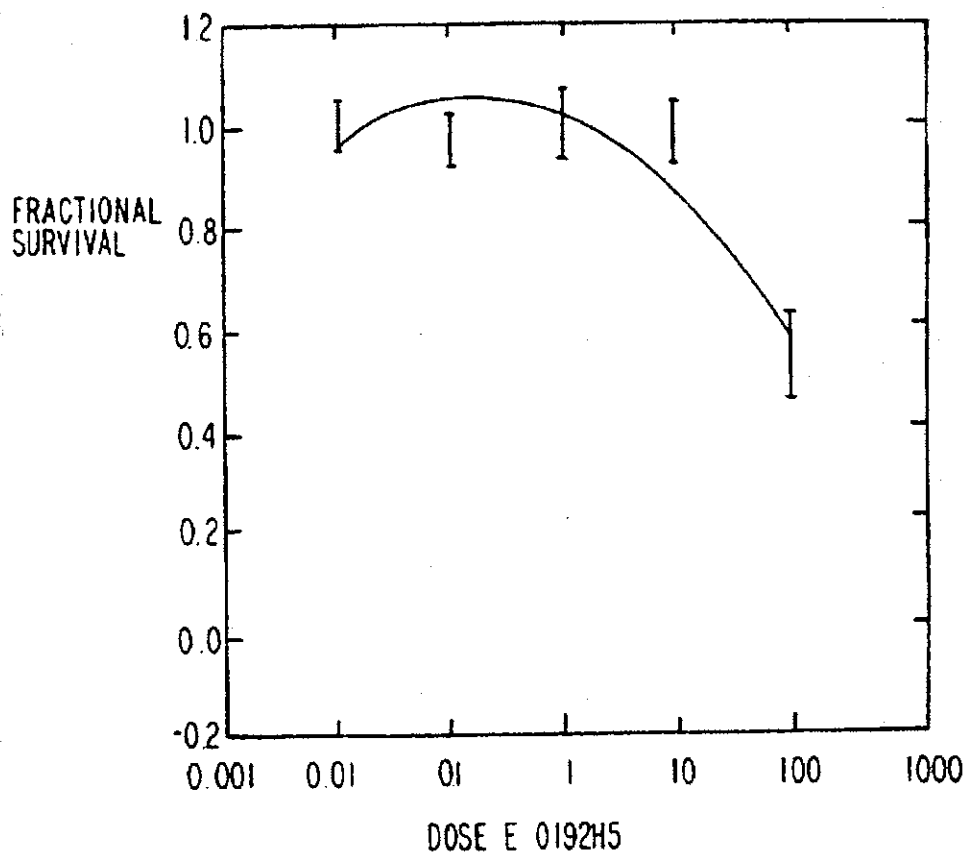


FIG. 9F

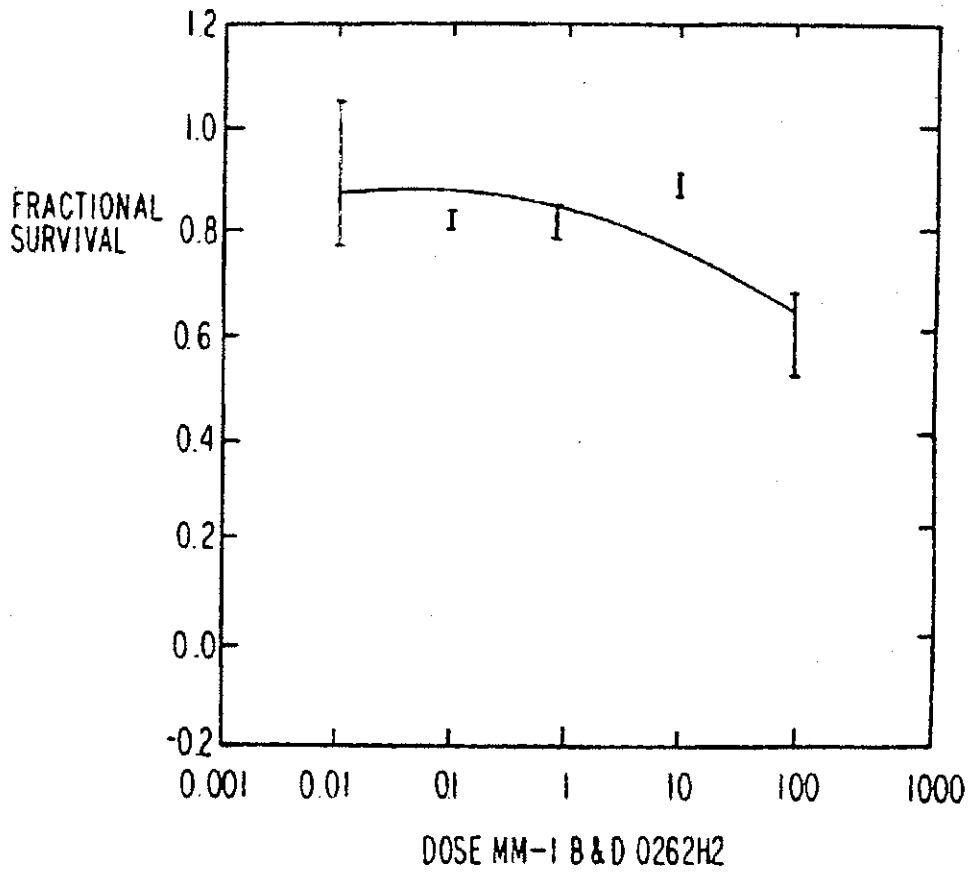


FIG. 9G

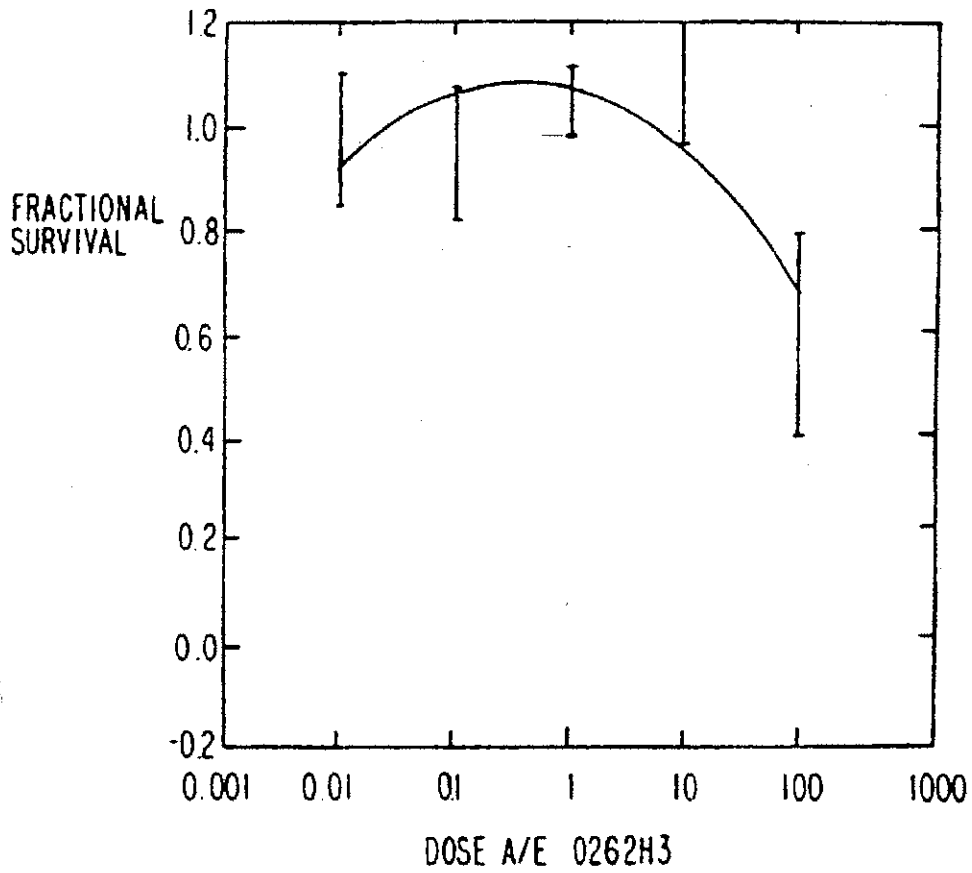
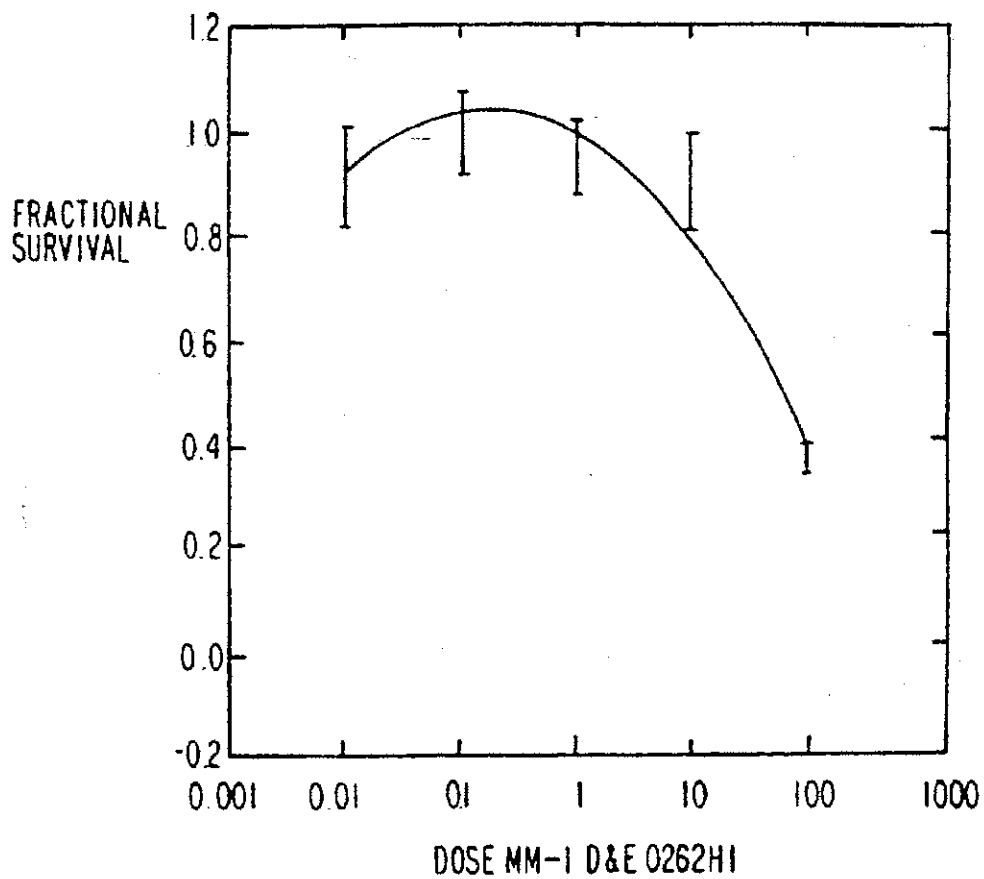


FIG. 9H



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FIG. 10A

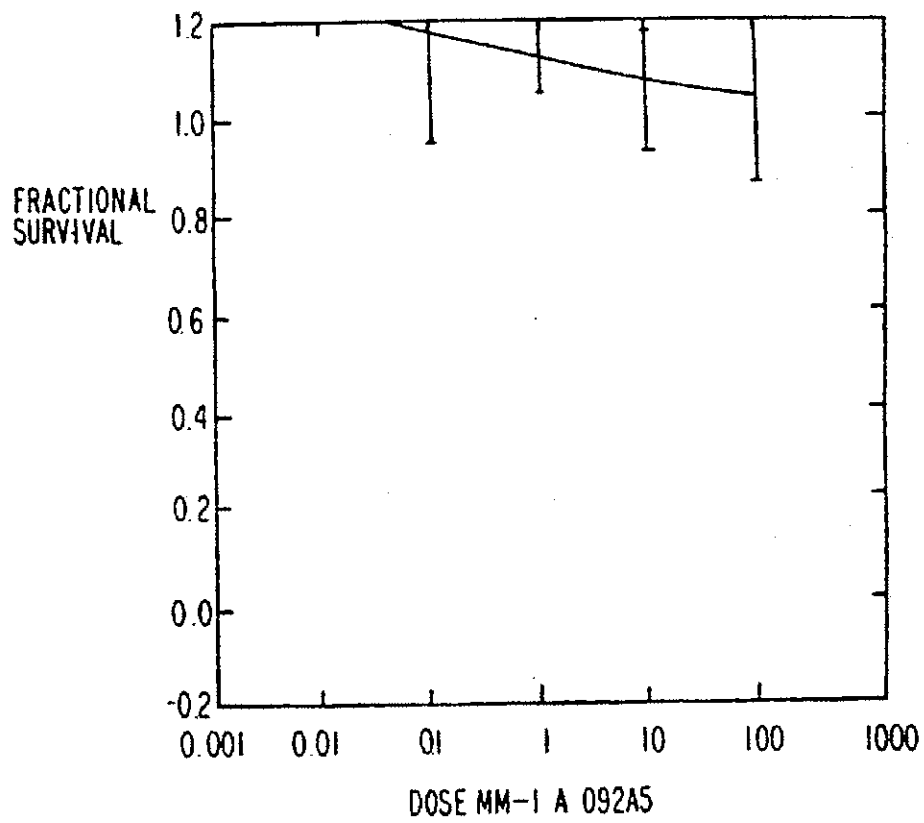


FIG. 10B

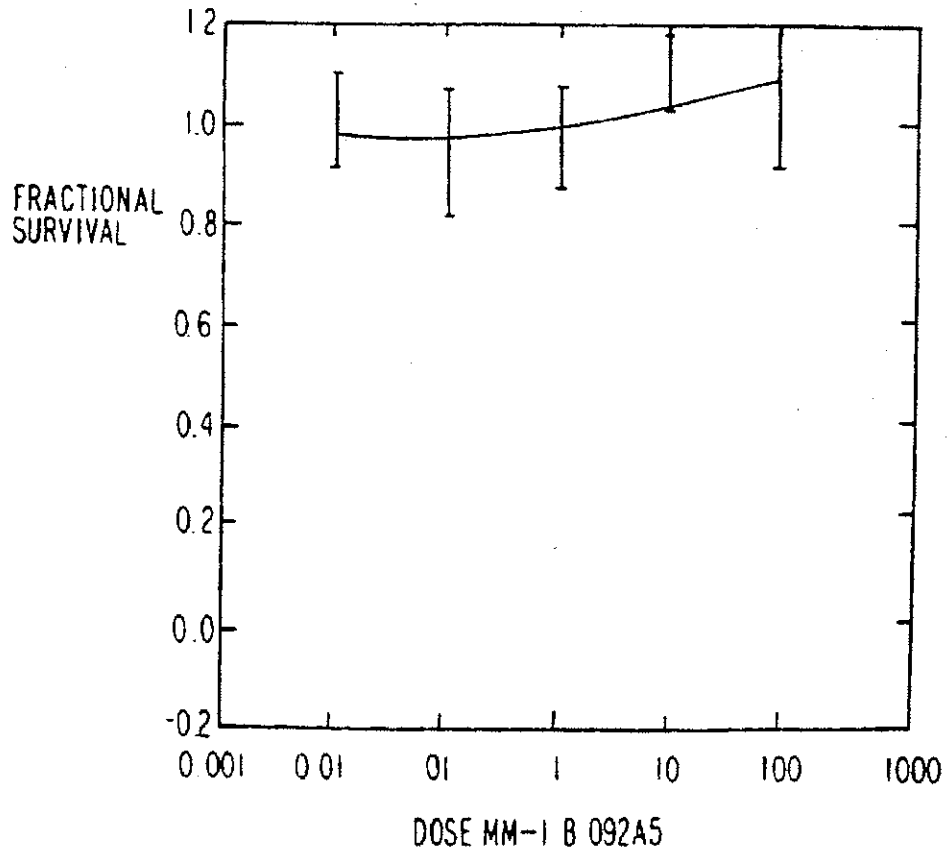


FIG. 10C

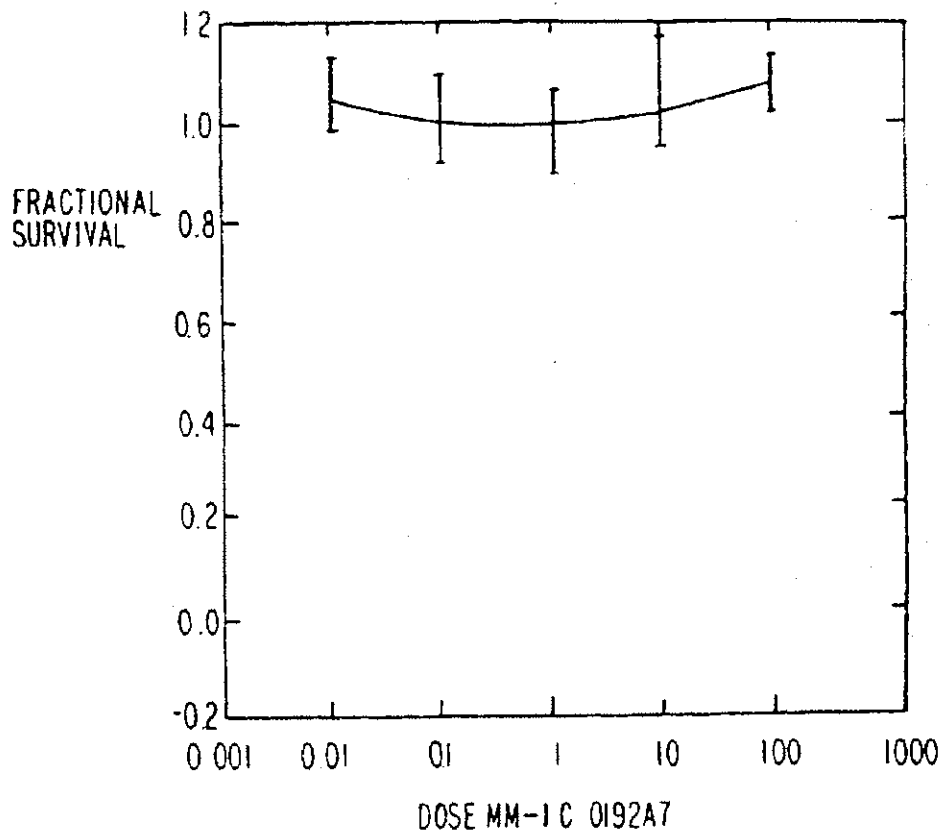


FIG. 10D

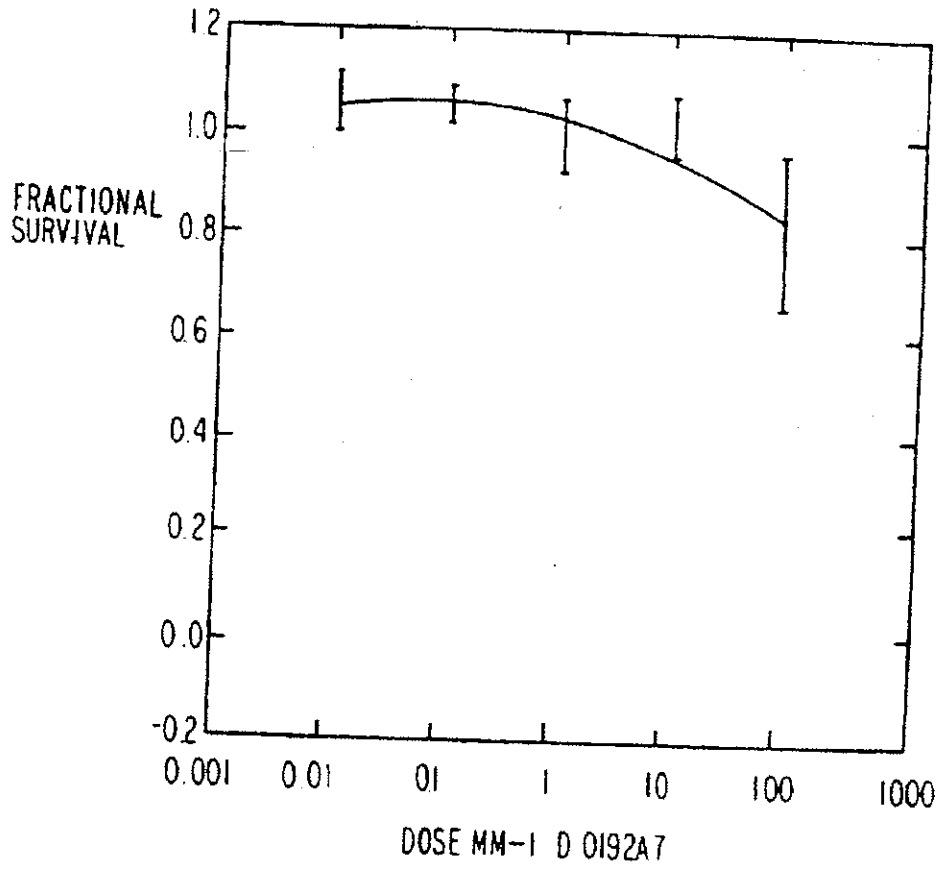


FIG. 10E

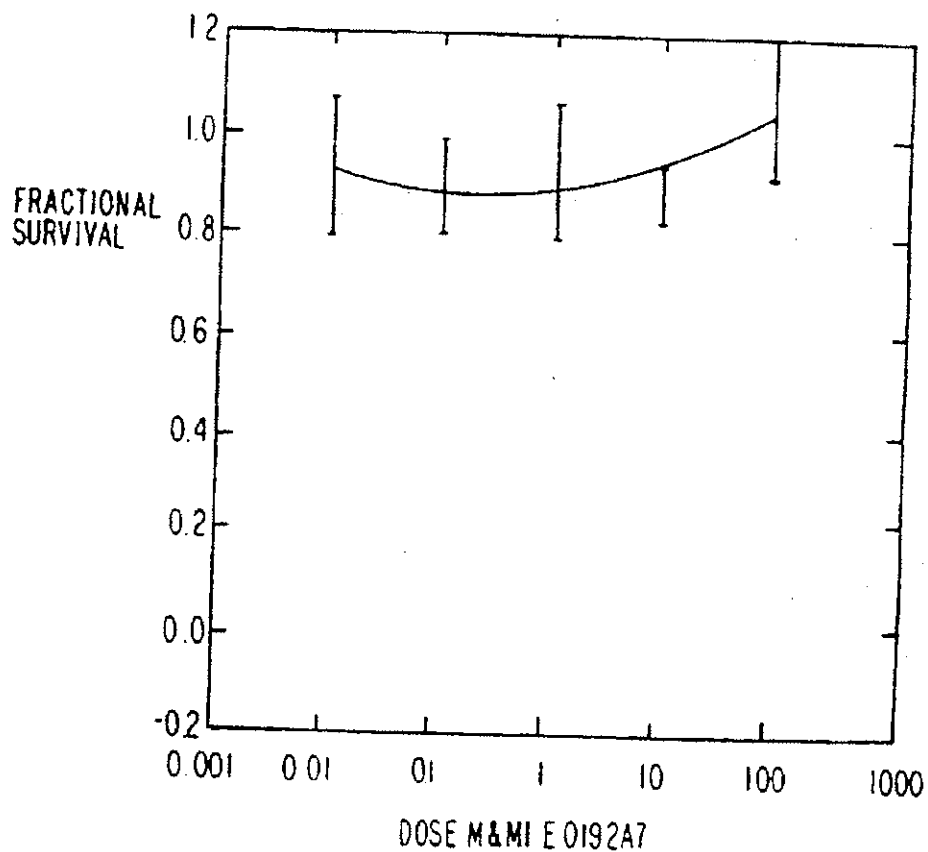


FIG. 10F

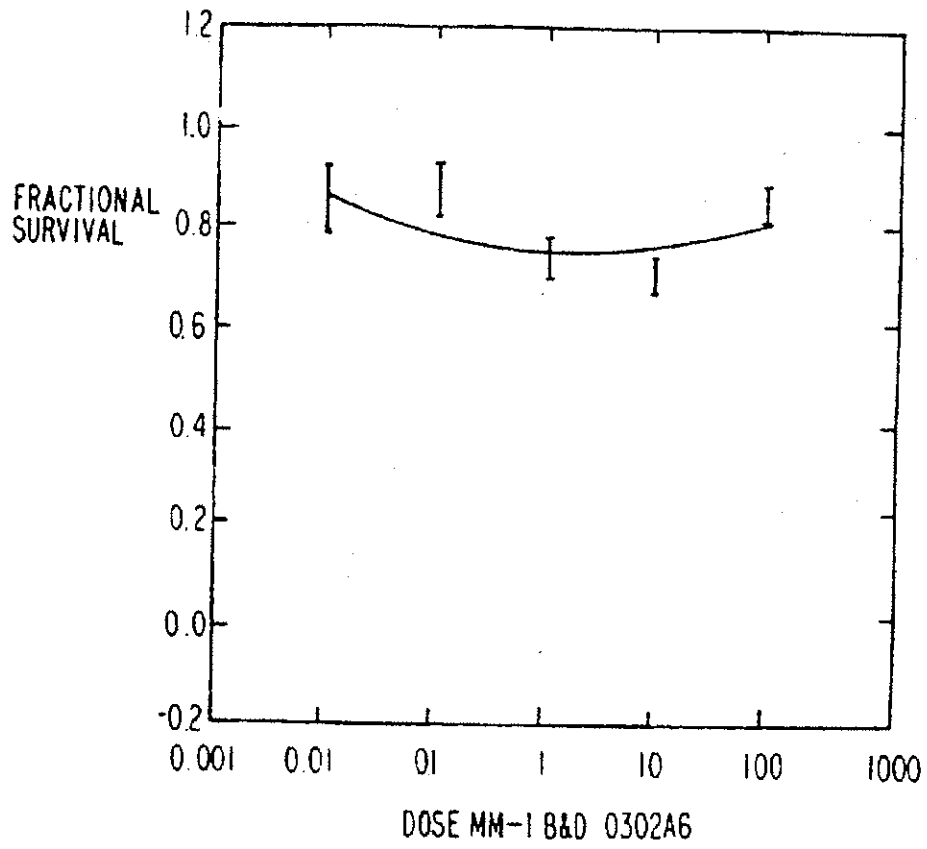


FIG. 10G

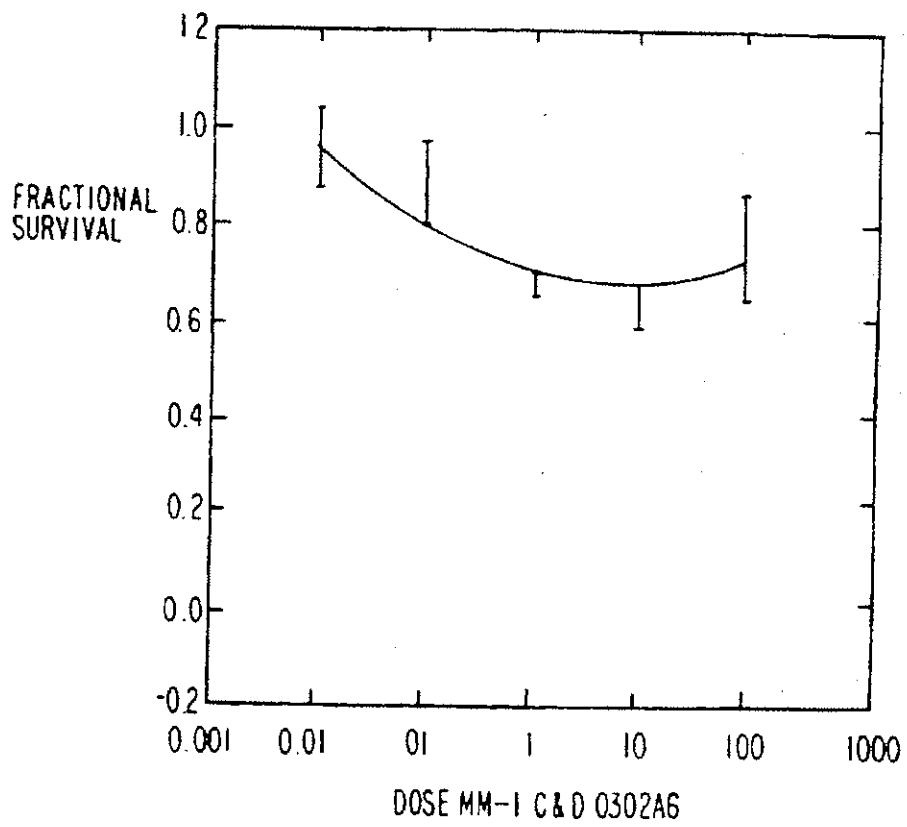


FIG. 10H

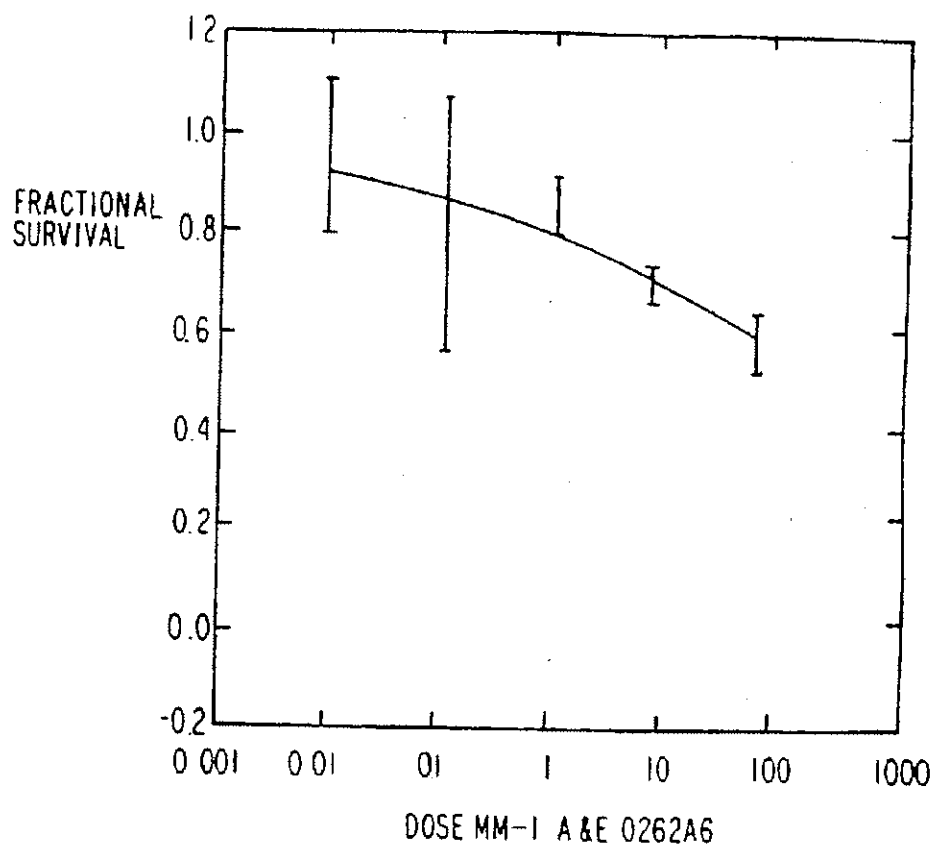


FIG. 11A

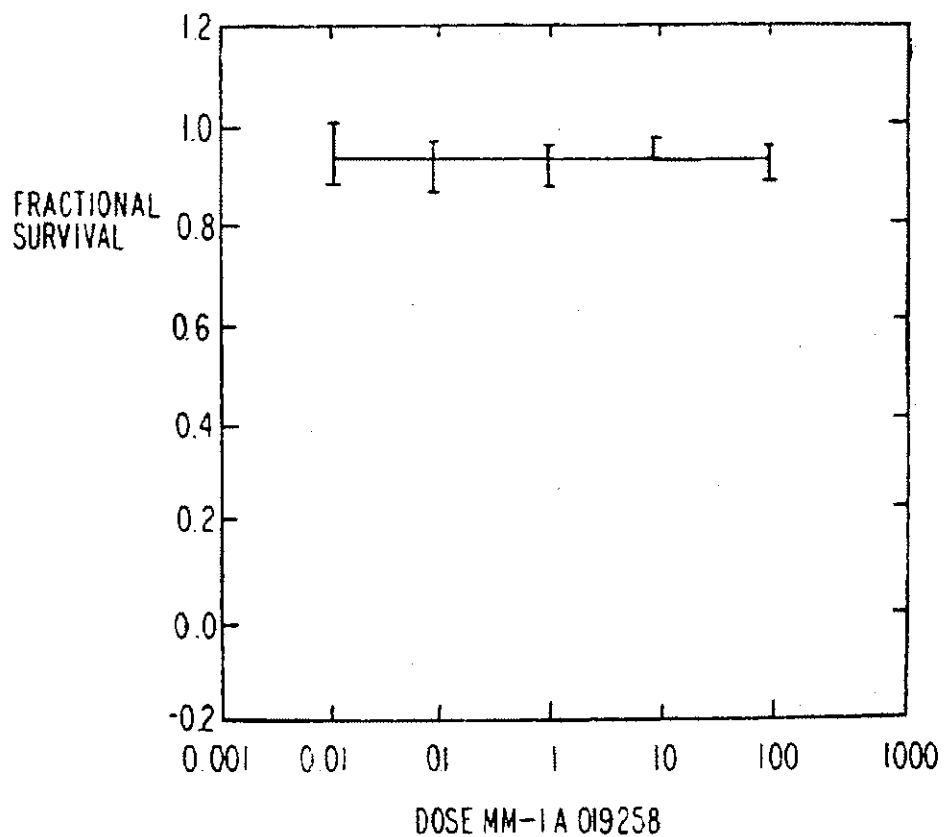


FIG. 11B

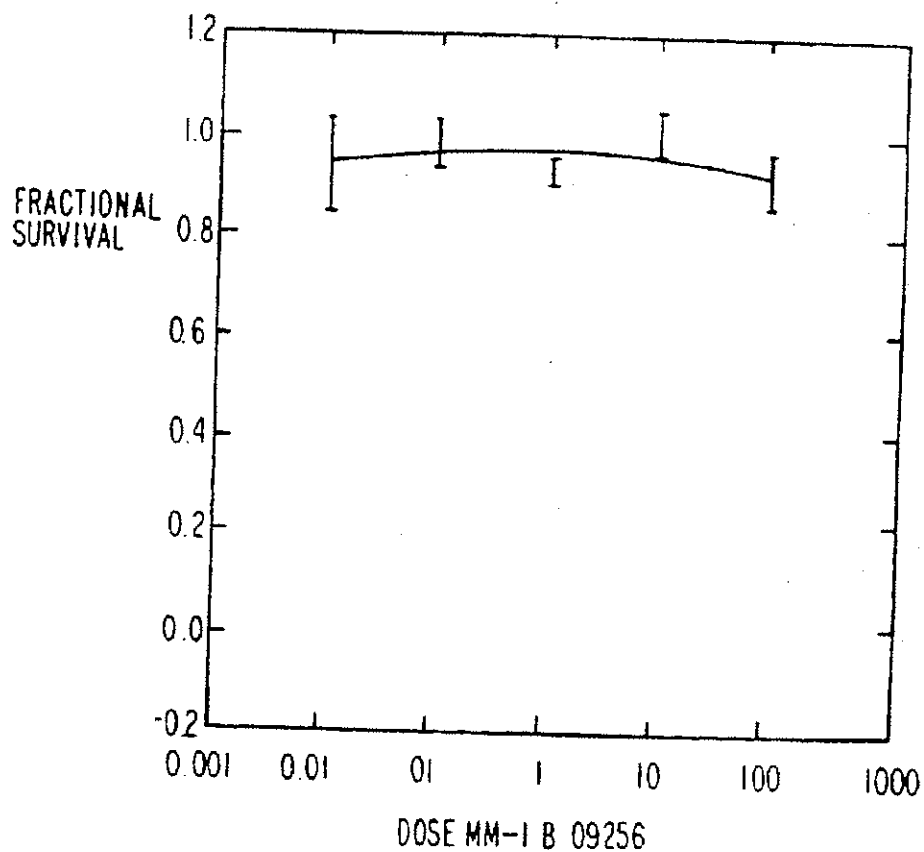


FIG. 11C

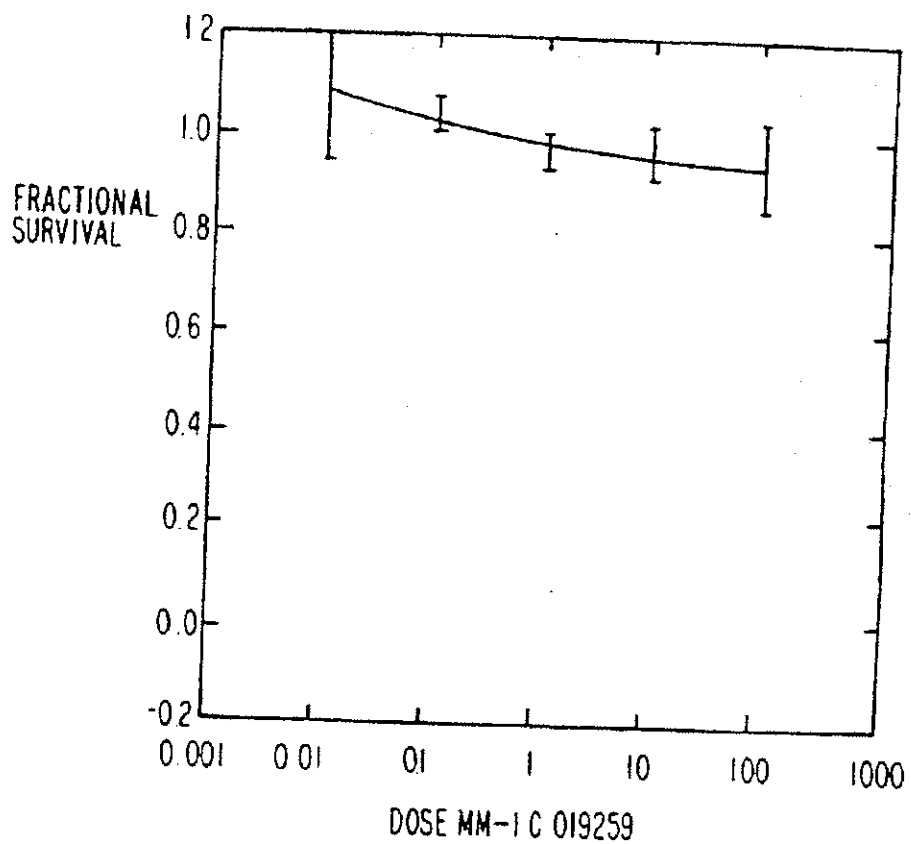


FIG. 11D

