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**Papadopoulos et al.**

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(54) **MODIFIED CHIMERIC POLYPEPTIDES  
WITH IMPROVED PHARMACOKINETIC  
PROPERTIES**

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WO WO99/03996 1/1999

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patent is extended or adjusted under 35  
U.S.C. 154(b) by 489 days.

This patent is subject to a terminal dis-  
claimer.

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(51) **Int. Cl.**  
**A61K 38/18** (2006.01)  
**C07K 14/71** (2006.01)  
**C12N 15/62** (2006.01)

(52) **U.S. Cl.** ..... **424/134.1; 424/192.1;**  
514/2; 514/12; 530/350; 536/23.4

(58) **Field of Classification Search** ..... None  
See application file for complete search history.

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(57) **ABSTRACT**

Modified chimeric polypeptides with improved pharmaco-  
kinetics are disclosed. Specifically, modified chimeric Flt1  
receptor polypeptides that have been modified in such a way  
as to improve their pharmacokinetic profile are disclosed.  
Also disclosed are methods of making and using the modi-  
fied polypeptides including but not limited to using the  
modified polypeptides to decrease or inhibit plasma leakage  
and/or vascular permeability in a mammal.

**7 Claims, 55 Drawing Sheets**

Fig. 1.

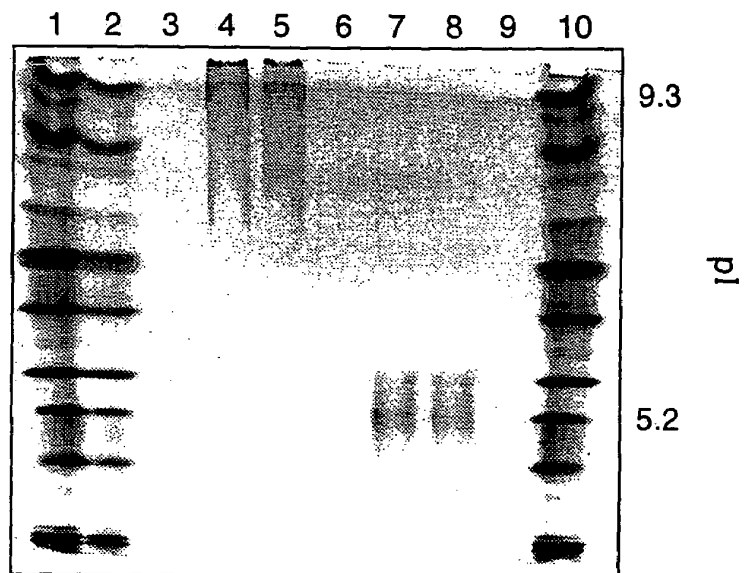


Fig. 2.

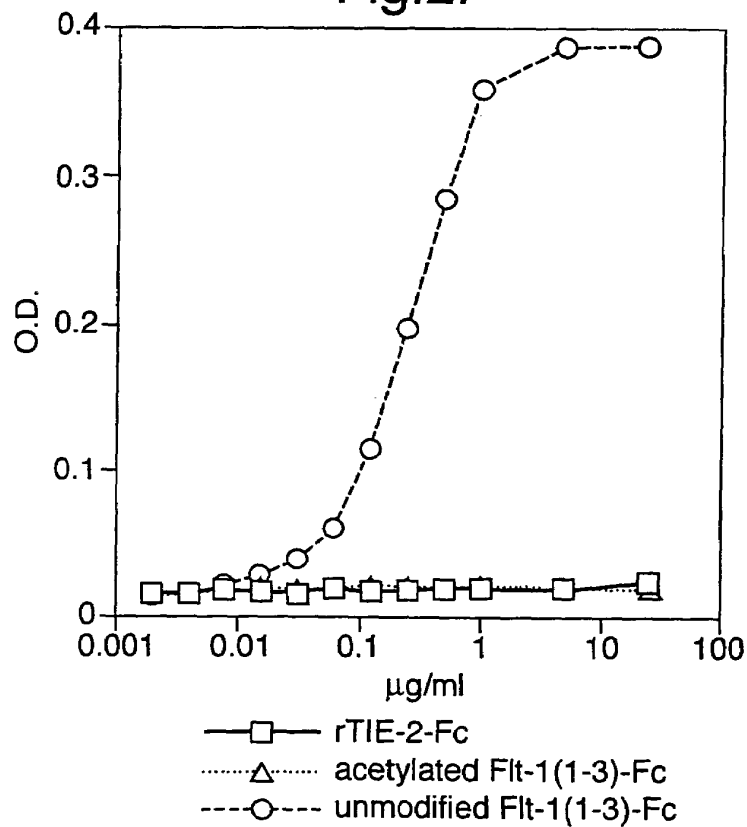
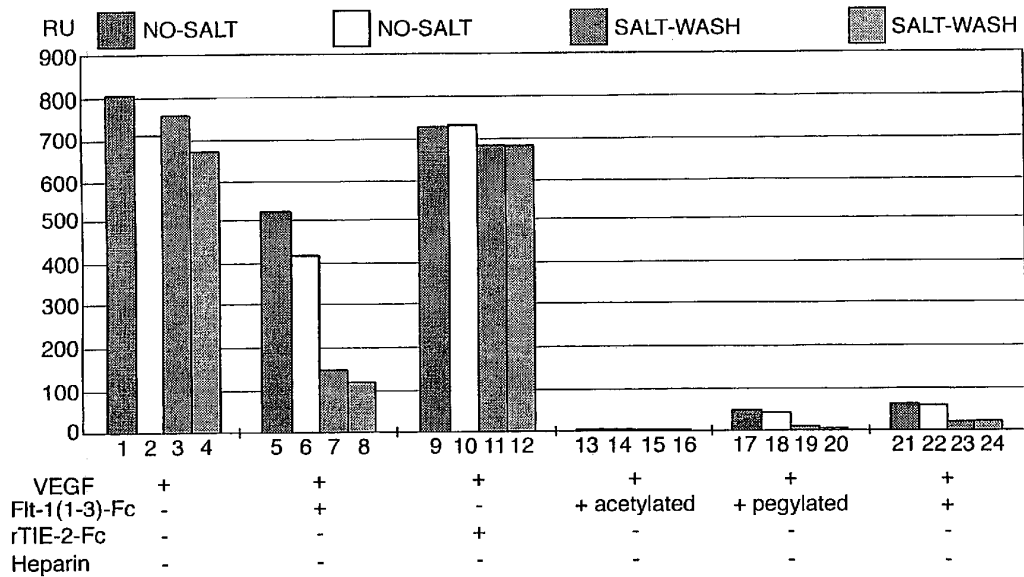
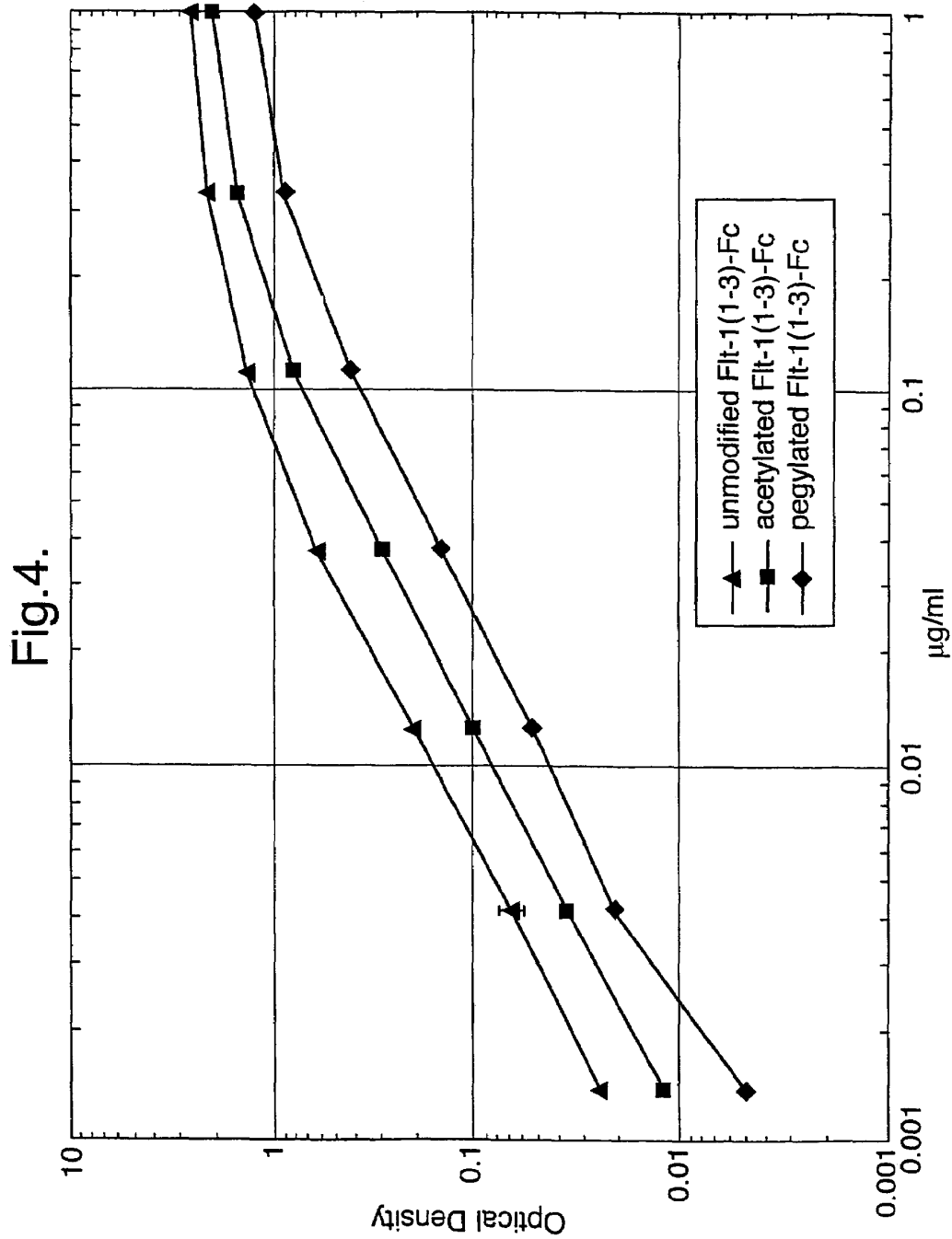
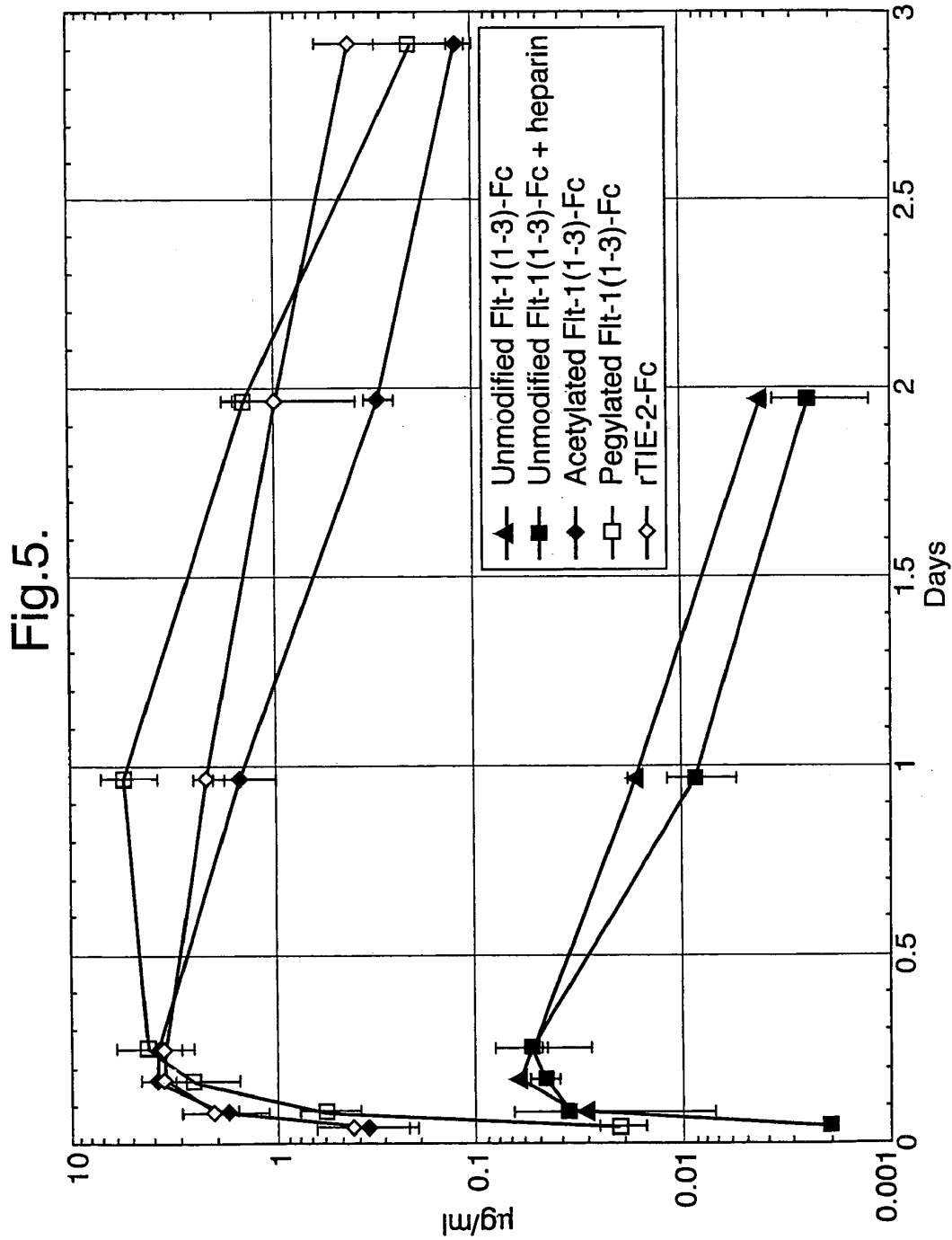


Fig.3.







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