Bull. Pharm. Sci., Assiut University
Vol. 10, Part 1, pp 1 - 36 (1987)

FORMULATION AND EVALUATION OF CERTAIN ANTI-INFLAMMATORY DRUGS FOR TOPICAL APPLICATION II-POLYMER FILM FORMS.

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ABSTRACT

The release characteristics of the nonsteroidal anti-inflammatory drugs, flufenamic and mefenamic acids from ethyl cellulose and polyvinylacetate polymeric cast films were studied.

The effects of formulation variables of the films composition viz, nonionic surfactants (Tween 80 and Span 20), and additive polymer (polypropylene glycol 2000 and polyethylene glycol 400) on the release characteristics of both drugs were also investigated. The effect of addition of hydroxypropylcellulose in different ratios to polyvinylacetate films at constant flufenamic acid concentration, on the release characteristics of the drug was also evaluated.

Further, the permeability properties of both free polymeric films for both drugs was evaluated and correlated with drug penetration through the skin of the rat, on the basis of the permeability constant and diffusion coefficient. Kinetic data analysis proved that the mechanism of release of both drugs followed a diffusion controlled model from the two polymeric films.

The release rate in pure and in mixed films was increased by Tween 80 or polyethylene glycol 400. Also release rate of flufenamic acid was increased markedly by inclusion of hydroxypropyl cellulose to polyvinyl acetate film to certain extent. Flufenamic acid release rate was always higher than that of mefenamic acid from both polymers. It was found that flufenamic acid had the higher diffusion coefficient than that of mefenamic acid.

INTRODUCTION

The design of controlled release dosage forms for transdermal drug administration is now a subject of considerable interest. However, only few quantitative studies have been done on such systems. Two basic physical models have been used to estimate drug release mechanisms: the membrane permeation controlled and the matrix diffusion-controlled (or the monolithic system) release[1].

Nevertheless, no attention has been paid to the topical drug delivery matrices, formed by casting technique and little investigated these drugs in skin permeation.

Drug release rates from polymeric films may be altered by variations in the formulation of the film[2], the polymer matrix material, plasticizers and the physicomechanical properties of the drug.

Donbrow et al[3] studied the effects of composition of cast films on the release behaviur of salicylic acid and caffeine and found that release rates were independent of film thickness and proportional to drug concentration in pure ethylcellulose films, and in the mixed films were altered by a change in the external fluid pH. They concluded that the release rate constant increased drastically with an elevation of the polyethylene glycol content of the film. Greater changes may be obtained by the use of additive polymers selected on the basis of hydrophilicity properties such as hydroxypropyl cellulose in polyvinylacetate films[4]. So, the objectives of the present work was to investigate the suitability of ethylcellulose and polyvinylacetate for formulation of topical controlled release drug delivery for flufenamic and mefenamic acids either as matrix film system or as controlling film laminate. In this concern, the effect of film formulation factors has been evaluated.

The objective of the work has been extended to compare the permeability of both polymeric films for both drugs with penetrability of these drugs to rat skin with the purpose of evaluation of the suitability of these film types as in-vitro model to predict percutaneous absorption of these drugs.

Flufenamic and mefenamic acids were used orally as effective anti-inflammatory drugs in the rheumatoid arthritis[5,6,7]. In the meantime they are known to be irritating to the gastrointestinal tract upon oral administration[6] and their limited solubility may prolong the contact time with the gastric mucosa, there by increasing their irritating action[7].

In a previous study, the formulation of these drugs in ointment forms has been attempted and proved to be effective to cure local induced inflammation[8].

Topical application of these drugs in inert polymer films affords possible method of achieving their effect as controlled drug delivery and avoiding intestinal irritation.

EXPERIMENTAL

Material and Methods:

Materials:

- Polyvinylacetate polymer (Searle Company, England).
- Ethyl Cellulose (had an ethoxyl content of 47.5 to 49.0%) (The Viscosity of 5% w/w solution in (80:20 w/w) toluene : ethanol was 14 CPS. The degree of Substitution 2.42 to 2.53), BDH chemicals Ltd, Poole, England.
- Flufenamic and Mefenamic acids were supplied by El-Nile company for Pharmaceutical and Chemical Industries, Egypt.
- Hydroxy propyl cellulose (4000), BDH.
- Tween 80, Merck, Span 20, ROTH, polyethylene glycol 400, BDH, polypropylene glycol 2000 (ROTH).

- Ethyl alcohol, acetone, and chloroform, all are of analytical or pharmaceutical grade (ADWIC)- and were used as received.

Film Preparation:

The films were cast from acetone solution containing 30% w/v ethyl alcohol and 2% w/v polymer, using the techniques of A.A.M. Abdel-Aziz et al[9]. Five milliliters of the prepared solutions were poured into circular Teflon molds (2 cm in diameter), and 5 mm in depth). The mold was covered with an inverted funnel to control solvent evaportion. Solvent was permitted to evaporate for 24 hours at room temperature. The composition of the films are given in Table 1. Films were prepared from chloroformic solution when the surfactants were inculded.

Film thickness was determined at ten random points on the film using digital micrometer and mean thickness was calculated ;(25 mm ± 0.£).

Mechanical studies of the polyvinylacetate films containing each of the two drugs were determined by measuring the linear expansion of standard free test film strips under increasing Load forces [10]

Determination of Release Rate :

The system developed for studying the drug release consists of double Teflon rings-shaped device, the diameter of each ring; 5 cm and the polymeric film was fitted in between these two rings and fixed with four screws. The membrane device was mounted on the surface of the release medium in beaker 150 ml; containing 50 ml of the release medium of isotonic phosphate buffer pH 6.8 at 37°C ± 0.5, by means of three filaments hanged from holder.

This situation generate the surface position of the membrane in the release medium and the continuous stirring of the medium using small magnet during the time of experiment. The exposed area of the membrane 25.142857 cm^2 Care of being the upper surface of the film facing the release medium was taken.

Aliquots (5 ml) were withdrawn at specified time intervals and replaced by fresh equal volume of the release medium. The amount of drug released

was determined spectrophotometrically (11) at the λ_{max} : flufenamic acid at 287 nm and mefenamic acid at 286 nm (both in isotonic phosphate, buffer, pH 6.8).

Kinetic Studies :

Drug release data from the medicated films were analysed according to the first-order kinetic, zero-order, and the diffusion-controlled model (12,13).

The values of intercept and slope were calculated by least square-procedure.

Diffusion Studies :

A diffusion cell consists of two conical chambers separated by the film under investigation[14]; the capacity of each chamber was 250 ml. The experiment was conducted in a thermostatically controlled water bath at 37°C ± 0.5.

Isotonic phosphate buffer pH 6.8 (150 ml) containing saturated solution of the drug, and buffer only, were simultaneously introduced into the donor and acceptor compartments respectively. Mixing in both compartments was conducted by magnetic stirring. The effective area of the membrane was 4.9 cm^2 between the donor and acceptor compartments.

Samples of five ml. were removed from the acceptor compartment at definite time intervals and the cumulative amount of drug penetrated was determined spectrophotometrically.

The diffusion experiments were done firstly using the unmedicated films of ethyl cellulose and polyvinylacetate; then secondly, the skin of the rat was used instead of the polymeric membrane for the two drugs. The apparent permeability constant $\bar{p}$ was calculated using the expression[15] $p = \frac{(do/dt)h}{c_d}$ where do/dt is the flow of the drug in a steady state regime and is obtained from the slope of the linear regression plot of the amount of the drug

penetrated versus time, and h is the matrix thickness and C_d is the initial donor concentration.

Skin Preparation[16]:

Excised abdominal skin of the male Wistar rats, 200-250 gm. were used. The skin was shaved on the epidermal side with a depilatory cream. Tissues on the dermal side up to and including blood vessels were removed. The skin was washed with distilled water and mounted in the diffusion cell between the two compartments. The skin thickness was measured with knowing that the thickness of the skin increased after hydration. The resulted concentration of the penetrated drugs were corrected using the difference in absorbance between the blank buffer removed from the acceptor compartment to exclude the compounds that entered from the skin membranes which thus had no effect on the accuracy of the determiation.

To evaluate the effect of polymeric type films on the drug penetration, the steady-state rate was determined and divided by the exposed area of the membrane to yield the penetration flux. The permeation data were used to calculate the diffusion coefficient of the drugs by means of the time lag equation of Barrer[17] and Daynes[18] $L= \frac{h^2}{6D}$ where L is the lag time in seconds and D is the diffusion coefficient, the solubility coefficient (S) can be calculated from the relation P=DS.

RESULTS AND DISCUSSION

Results of release experiments with two drugs of nearly the same molecular weight from two polymeric films of widely varying molecular size and hydrophilicity are presented in (Fig. 1-4) and Tables (II, III).

From Tables (II, III) it is seen that the kinetic constant characterisitcs of the drug/polymer system (K); are increased relatively with increasing the concentration of the drug in the film. This result is in agreement with the first order release model.

However, when the amounts of the drug released were plotted against the square root of time, straight lines were also obtained (Fig. 5-8) and Tables (IV,V).

Since both first-order and square root of time plots are acceptably linear, a more stringent test was needed to distinguish between the mechanisms.

The two mechanisms were differentiated by plots of rates as function of Ø (amount released per unit surface area) and of 1/Ø, because the plots of rate versus 1/Ø proved to be linear (Fig.9) and those of rate versus Ø curved throughout the whole of the release period, indicating that the process is diffusion controlled.

Plots of log Ø against log t were linear for both drugs, confirming the diffusion model (Fig. 10).

Further more, the increase in release rate as the quantity of the drug increased agreed with the investigations of Donbrow and Friedman[18] for the release characteristics of salicylic acid and caffeine from ethyl cellulose films only.

Influence of the Drug Type:

The release rates of flufenamic and mefenamic acid from identical films, Viz, films based on ethyl cellulose or polyvinylacetate, demonstrate, that the solubility of the drug, although not affecting the release mechanism, has a marked influence on the release rate. On the basis of the slopes of the diffusion-controlled curves Tables (IV, V), the release rates of 1% flufenamic acid (soluble drug)[11] from polyvinylacetate are much higher than the release rate of 1% mefenamic acid from the same polymer film and the same pattern for ethyl cellulose film.

Influence of Base Polymer Type:

From Tables (IV,V), it is obvious that the base polymer may exert an influence on the release rate.

For a sparingly soluble drug as mefenamic acid, the release rate increases to a marked extent if the base polymer of the film has a certain swelling properties and forming channels as ethyl cellulose except at concentration 3%.

The data obtained with flufenamic acid showed that the release rate increased from polyvinylacetate films excepted concentration 1%.

The above results demonstrated the phenomenon that the greater the difference in solubility of drug and base polymer, the higher the release from the film. Also, these results may be due to the difference in crystallinity of the two polymers[19].

Influence of Additive Polymer:

Addition of hydrophilic substance to a hydrophobic polymer film is one of the methods by which the release properties of the film can be increased[20].

The release rates of fulfenamic acid 1% from polyvinylacetate films containing different ratios of hydroxypropyl cellulose, demonstrate that release of drug increased with increaseing hydrophilicity of the matrix.

The addition of polar substituents leading to an ordered structure to the non-ordered one[19].

It might be expected that increasing the ratio of water soluble substance in the formulation would have an effect higher than decreasing the ratio of it.

This was not found to be the case with flufenamic acid release as shown from Table (VI) and (Fig. 11).

These results may be due to the hydrophilic effect of polymer with its enhancing effect on release rate of the drug is counterbalanced with the increase viscosity in channels which retard diffusion of the drug.

Release of flufenamic acid from ethyl cellulose films containing 20% polyethylene glycol 400 and 20 % polypropylene glycol 2000 was investigated (Fig. 12), depicts that polyethylene glycol 400 is more effective in enhancing release rate of the drug from ethyl cellulose than polypropylene 2000. This may be attributed to the higher leachability and solubility of polyethylene glycol 400 forming channels in the film through which the drug is released.

Influence of Non-Ionic Surfactants :

The release data of flufenamic and mefenamic acids in presence of 0.6% of Tween 80 or span 20 (Fig. 13,14) demonstrate that major differences in the nature of an incorporated surfactant did not influence the mechanism of drug release however Tween 80 increased the release rates of both drugs from ethyl cellulose films while span 20 slightly decreased the release rate. The increase in release rate of flufenamic acid may be attributed to the difference in hydrophilicity and solubility of both surfactants and their effects on drug solubility[20].

Mechanical Properties in Relation to Drug Type:

It was interest to characterize the topical films of polyvinylacetate in terms of its mechanical properties. The stress-strain curves of the films containing 1% flufenamic or mefenamic acids were determined (Fig. 15).

It appears from Table (VII) that flufenamic acid increases the stress on the film and films showing little deformation and being hard and strong while mefenamic acid imparts toughness to the film. It was also shown that tensile strength did not affected by the incorporation of drug.

Drug Permeation:

Permeation of flufenamic and mefenamic acids through films was ivestigated at 37° ±2 in relation to formulation variables. The variables involved were the base polymer, the additive polymer and the drugs.

The additive polymer considered was polyethylene glycol 400, to enhance the permeability of mefenamic acid in the film.

Given the permeation rate constant (P) from the experimental results and the calculated diffusion coefficient (D), it was possible to calculate the solubility coefficient (S) of the drug from equation (P = DS).

The values of permeability constant, diffusion coefficient and solubility coefficient are presented in Table VIII in relation to formulation variables.

The data in Table VIII showed that the rank of order of membranes in terms of their permeability constants was generally, very similar to that in terms of solubility coefficient.

The influence of polyethylene glycol 400 with regard to mefenamic acid permeation (Fig. 16) can be interpreted in terms of its effect as solubility modifiers in the film.

Polyethylene glycol 400 increased the permeation rate constant of mefenamic acid as long as it increase the solubility coefficient of the drug and also because it had the capability of enhancing the porosity of the films, once are leached and left capillaries behind, reducing, thus, the effective thickness of the film. This pointed to that mefenamic acid could be permeate via the aqueous pores of the film.

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Generally, mefenamic acid permeated from ethyl cellulose more rapid than from polyvinylacetate. Also, the permeability constant of flufenamic acid from ethyl cellulose was higher than that from polyvinylacetate.

The penetration flux rate of mefenamic acid was higher than that of flufenamic acid through rat skin.

Accordingly, the choice of drug, polymer film and inclusion of additive polymer had a marked influence on the release characteristics and permeability of drugs from and through polymeric film.

Under the conditions of this study, it has been observed that there is no correlation between data of flufenamic and mefenamic permeation through ethyl cellulose and polyvinylacetate films and their permeation through rat skin.

This can be attributed to the difference in skin thickness, solubility of both drugs and its composition from the polymeric films.

Table 1 : Film Composition and Preparation

Polymer	Ehtyl Cellulose 2 Gm/100 ml Polyvinyl acetate Casting Solvent*	
Drug	Flufenamic Acid Different Conc. Mefenamic Acid (1- 3%)	
Surfactant	Tween 80 (0.6% w/w) of Polymer) Spon 20 (0.6% w/w) of polymer)	
Additive Polymer	Polyethylene Glycol 400 (20% w/w) Polypropylene Glycol 2000 (20% w/w) Hydroxypropyl Cellulose (0.1, 0.2, 0.5%)	
Method of Preparation	Casting Technique	
* Casting Solvent	Acetone Containing 30% Ethyl Alcohol.	

Table II: Effect of Concentration of Flufenamic Acid Released From Ethyl Cellulose Films

Drug Conc. w/w	Correlation Coefficient	Release Rate	$t_{\frac{1}{2}}$(hr.)	Intercept
1.0 %	0.9953	0.0493	14.056	3.4034
1.5 %	0.9741	0.1001	6.923	3.2702
2.0 %	0.9695	0.2176	3.1838	3.1608
3.0 %	0.9712	0.2154	3.2167	3.6257

Effect of Concentration of Mefenamic Acid Released From Ethyl Cellulose Films

Drug Conc. w/w	Correlation Coefficient	Release Rate	$t_{\frac{1}{2}}$(hr.)	Intercept
1.0 %	0.9789	0.1030	8.728	3.0835
1.5 %	0.9982	0.0852	8.1310	3.2405
2.0 %	0.9985	0.0811	8.5378	3.3829
3.0 %	0.9986	0.0506	13.7006	3.5652

Table III: Effect of Concentration of Flufenamic Acid Released From Polyvinylacetate Film

Drug conc. w/w	Correlation Coefficient	Release Rate	$t_{\frac{1}{2}}$(hr.)	Intercept
1.0 %	0.9973	0.0937	7.3917	3.0993
1.5 %	0.9915	0.2274	3.0465	3.2853
2.0 %	0.9722	0.4273	1.6218	3.5240
3.0 %	0.9673	0.3253	2.1298	3.6265

Effect of Concentration of Mefenamic Acid Released From Polyvinylacetate Films

Drug conc. w/w	Correlation Coefficient	Release Rate	$t_{\frac{1}{2}}$(hr.)	Intercept
1.0 %	0.9935	0.0747	9.2737	3.0919
1.5 %	0.9955	0.0551	12.5586	3.2491
2.0 %	0.9977	0.0466	14.857	3.3948
3.0 %	0.9958	0.0624	11.0915	3.5713

Table IV : Effect of Concentration of Flufenamic Acid on the Release From Ethyl Cellulose Films

Drug Conc. w/w	Correlation Coefficient	Release Rate	Intercept
1.0 %	0.9813	12.6068	8.5480
1.5 %	0.9590	15.972	11.512
2.0 %	0.9685	19.6904	14.612
3.0 %	0.9740	56.677	38.34

Effect of Concentration of Mefenamic Acid on the Release From Ethyl Cellulose Films

Drug Conc. w/w	Correlation Coefficient	Release Rate	Intercept
1.0 %	0.9949	11.2136	5.1422
1.5 %	0.9945	14.0982	5.6089
2.0 %	0.9960	18.9178	7.4951
3.0 %	0.9928	19.3190	8.5335

Table V : Effect of Concentration of Flufenamic Acid on the Relase From Polyvinylacetate Films

Drug conc. w/w	Correlation Coefficient	Release Rate	Intercept
1.0 %	0.9915	10.8679	6.2732
1.5 %	0.9937	28.2785	16.2128
2.0 %	0.9909	53.399	35.67
3.0 %	0.9878	66.0257	31.9919

Effect of Concentration of Mefenamic Acid on the Release From Polyvinylacetate Films

Drug conc. w/w	Correlation Coefficient	Release Rate	Intercept
1.0 %	0.9851	6.3083	1.4083
1.5 %	0.9869	9.9886	4.8580
2.0 %	0.9887	12.0940	6.4811
3.0 %	0.9854	23.1839	12.4208

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Table VI: Release Characteristics of Flufenamic Acid from Polyvinylacetate Films Containing Different Ratios of Hydroxypropyl . Cellulose

Polymer Ratio		Correlation Coefficient	Release Rate	Intercept
PVA*	HPC**			
2.0	0.0	0.9915	10.8679	0.2732
1.9	0.1	0.9966	19.8988	8.7982
1.8	0.2	0.9939	18.8710	10.4100
1.5	0.5	0.9857	18.6488	11..9232

* PVA: Polyvinylacetate

** Hydroxypropyl Cellulose

Table VII :Effect of Drug on the Mechanical Properties of the Polyvinylacetate Film.

Drug Conc. 1%	Tensile Strength kg/cm^2	%Elongation at Break	Breaking Load
- Flufenamic acid	293.2	800	14.66
- Mefenamic acid	266.0	875	13.33

Table VIII: Correlation of Drug Permeability and Diffusion Coefficient Through Polymeric Films and Skin of the Rat

Drug	cm^2 5-1 Polymeric Film	cm^2 5-1 Permeability Constant $x10^{-2}$ Exp*	Penetration Flux Rate (Slope)	Diffusion Coefficient cm^2/h	Solubility Coefficient Calculated**	Lag time (Sec)	Thickness of mm Polymeric Film
Flufenamic Acid	PVA	0.06429	0.0170	$0.62x10^{-6}$	0.30	1417.4464	0.25
Mefenamic Acid	PVA/(PEG)***	1.11632	0.0366	$0.52x10^{-6}$	4.20	1770.1657	
,,	PVA	0.21343	0.1185	$0.27x10^{-6}$	0.86	1641.8154	
Flufenamic Acid	EC	0.72359	1.9942	$0.47x10^{-6}$	1.86	2589.7716	
Mefenamic Acid	EC	1.38213	0.7678	$0.35x10^{-6}$	10.36	889.0148	
Flufenamic Acid	Skin	0.54963	3.0771	$5.40x10^{-6}$	$0.8x10^{-6}$	51840	Whole thickness 0.5 cm
Mefenamic Acid	Skin	0.25547	4.2616	$5.92x10^{-6}$	$0.6x10^{-6}$	49989.4	

* Permeability Constant Experimentally Calculated.

** Solubility Coefficient Calculated from Equation

*** Polyethylene Glycol 400

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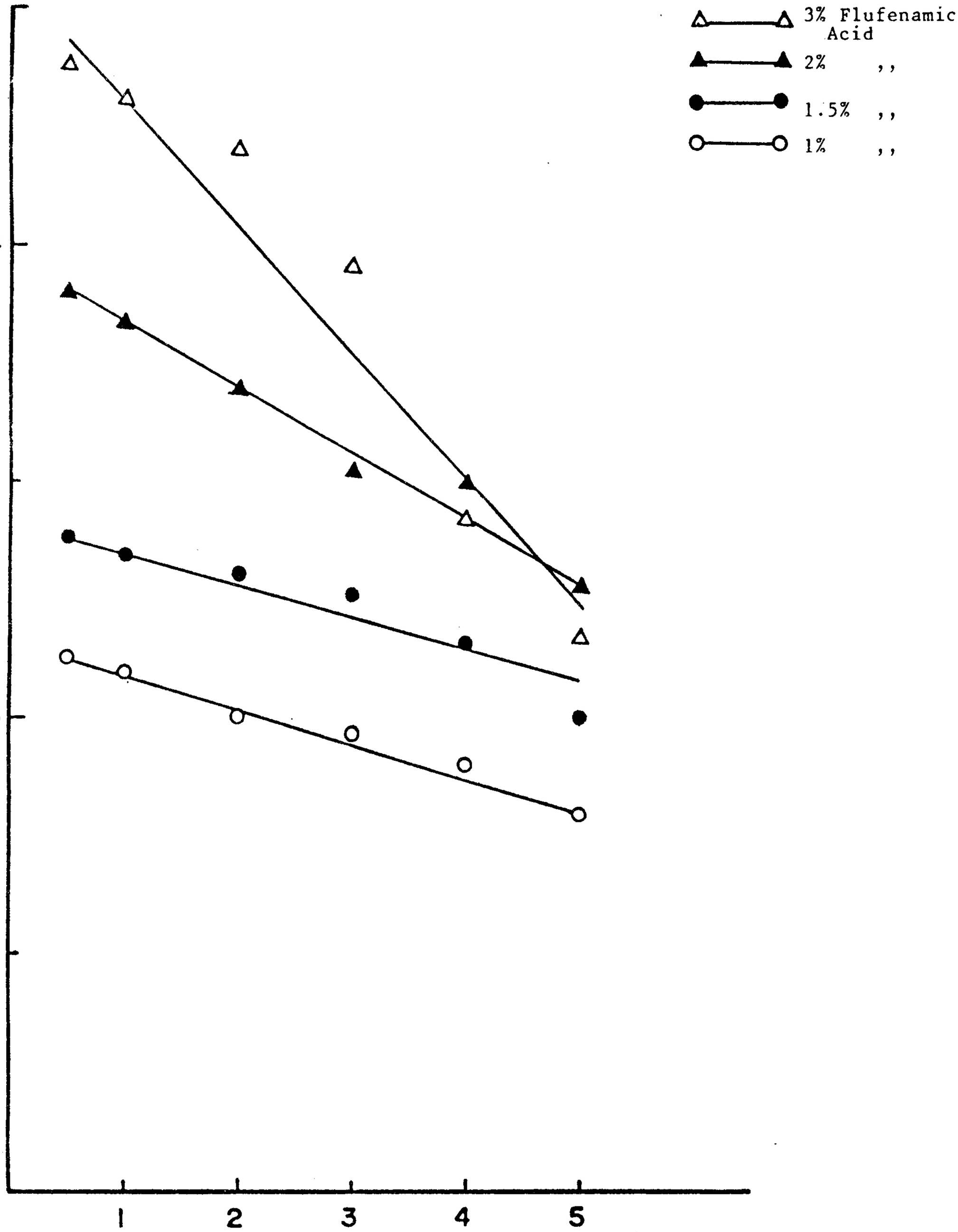

Fig. 1: Release of Flufenamic Acid from Ethyl Cellulose Films in Isotonic Phosphate Buffer PH 6.8

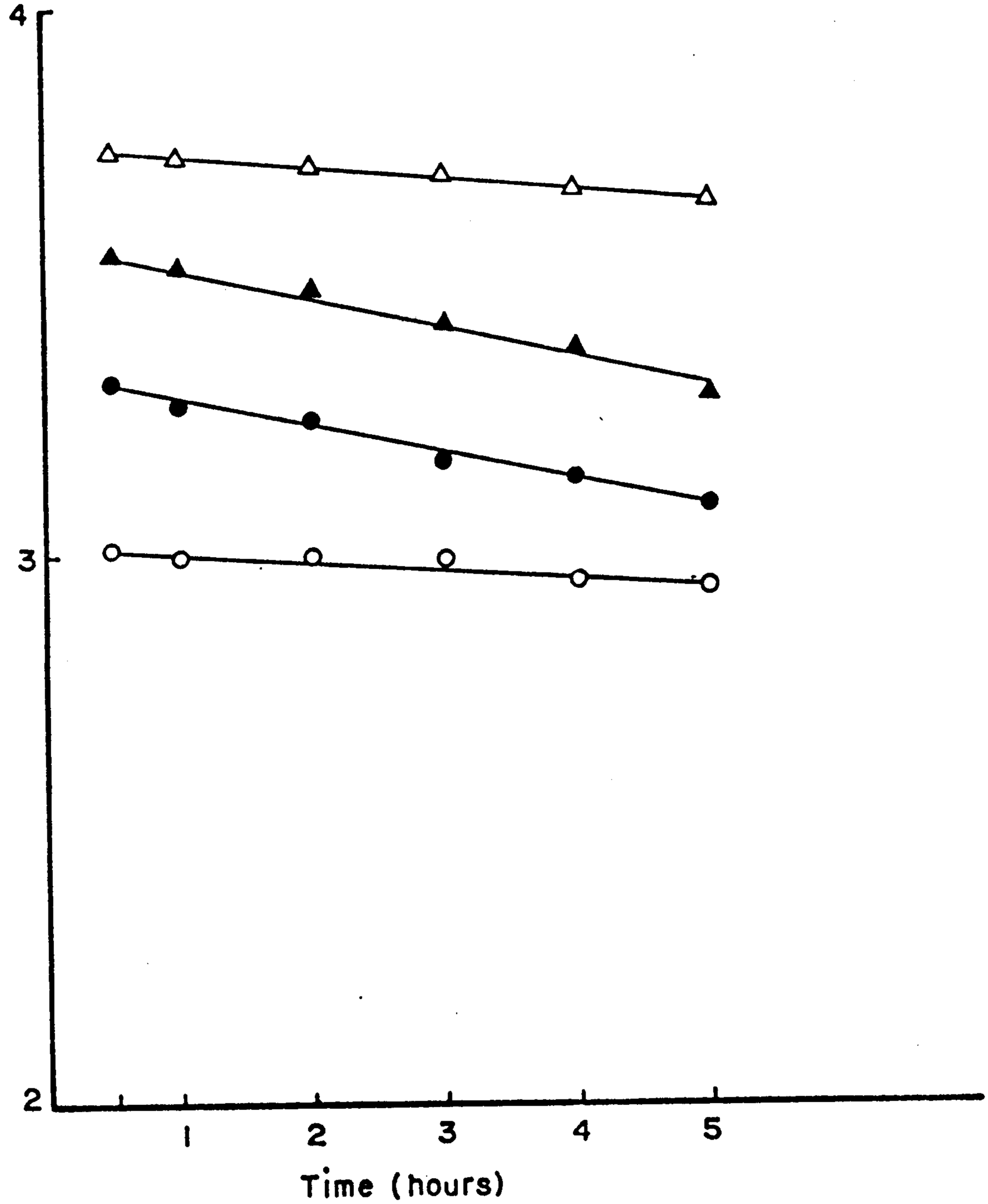

Fig. 2 : Release of Mefenamic Acid from Ethyl Cellulose Films in Isotonic Phosphate Buffer PH 6.8

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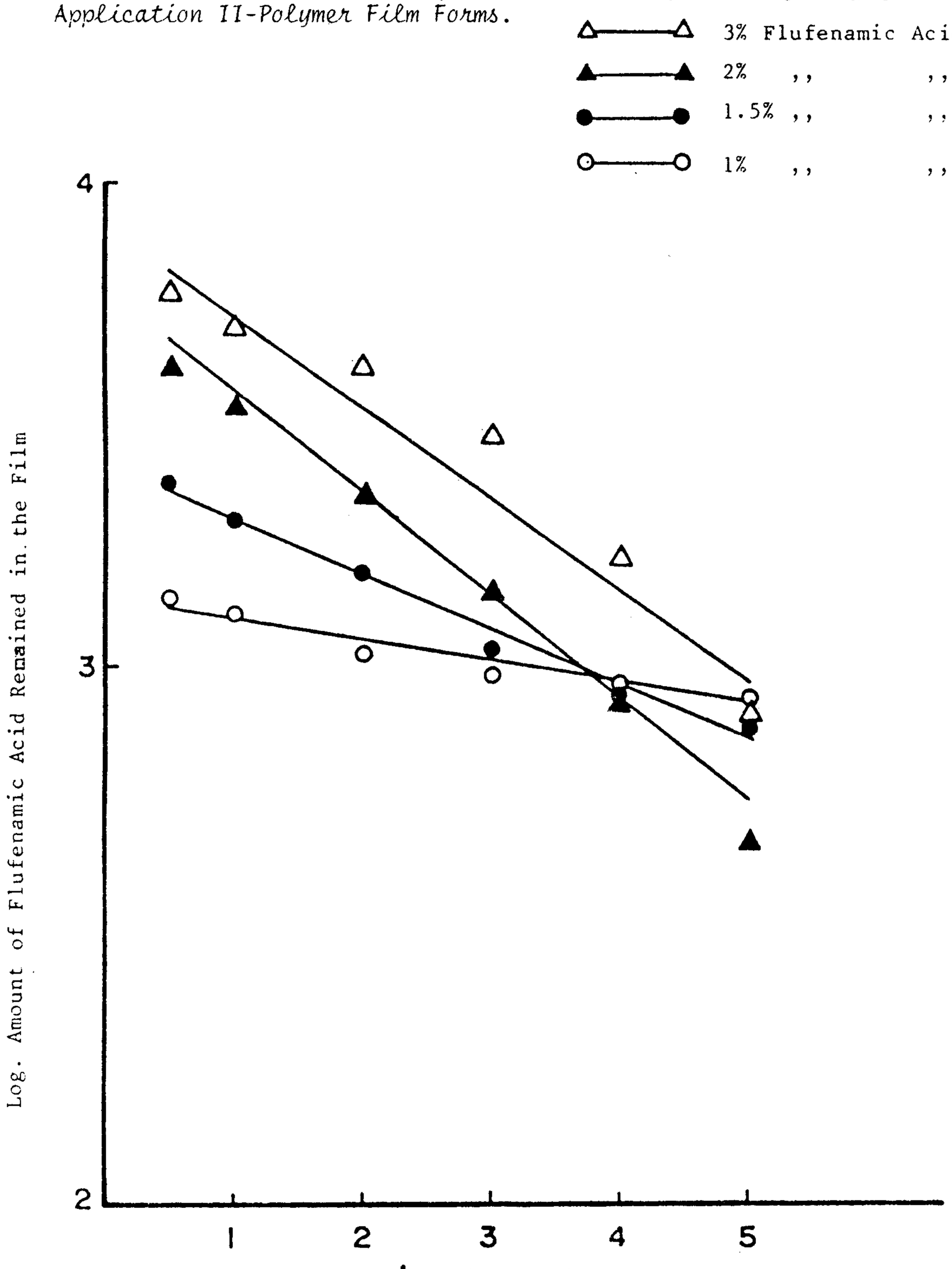

Fig. 3 : Release of Flufenamic Acid from Polyvinyl-acetate Film in Isotonic Phosphate Buffer PH 6.8

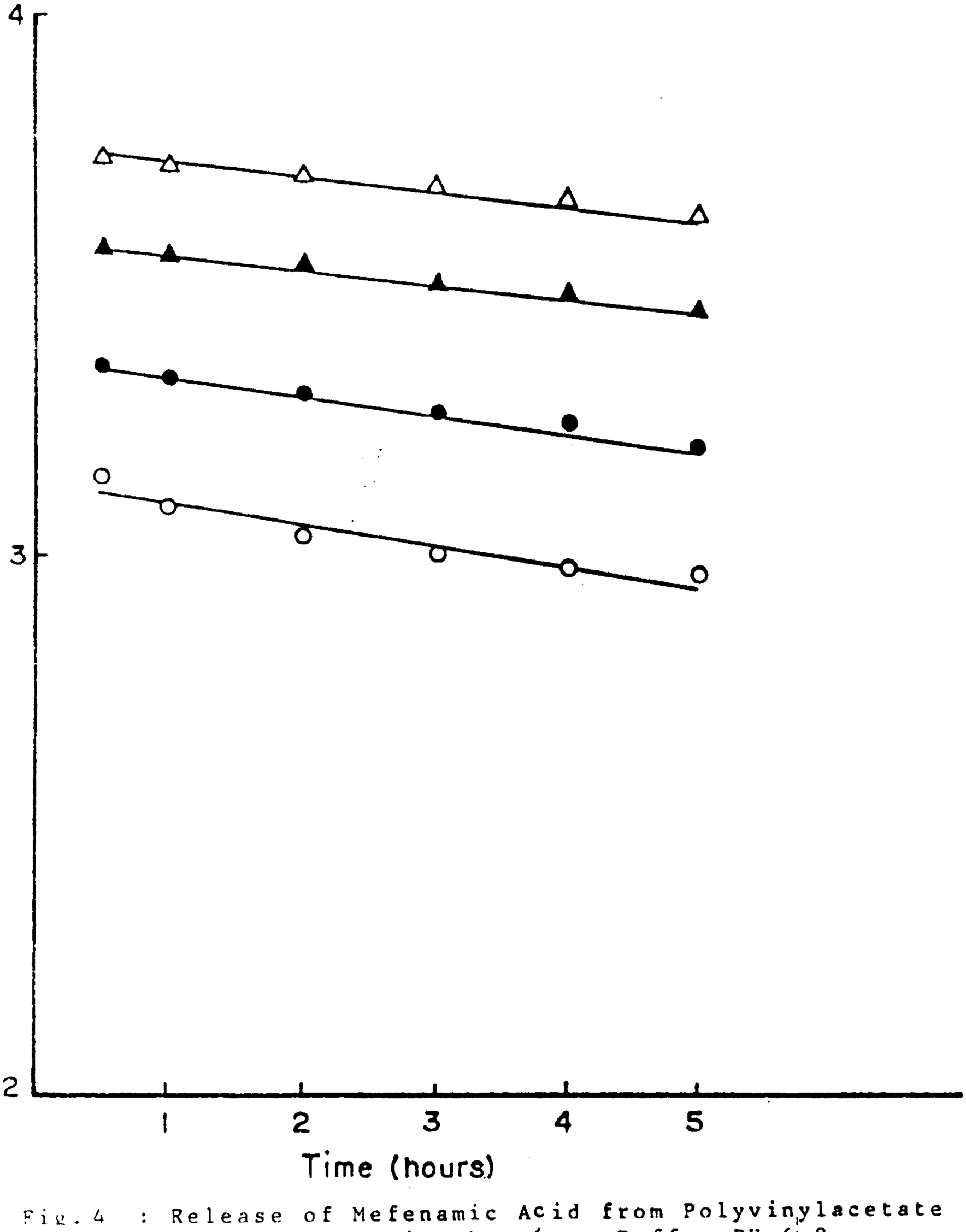

Fig. 4 : Release of Mefenamic Acid from Polyvinylacetate Film in Isotonic Phosphate Buffer PH 6.8

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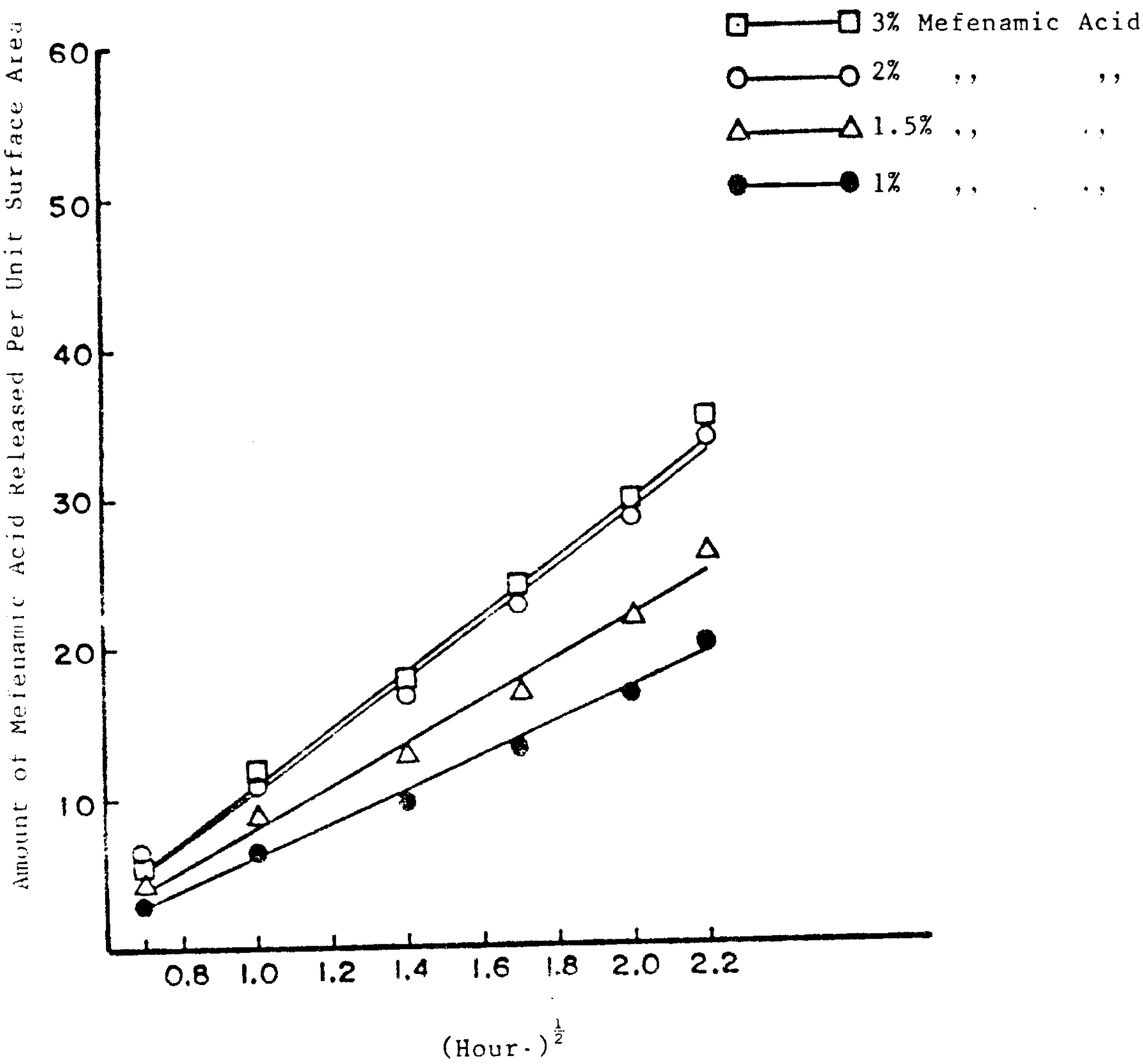

Fig. 5 : Release of Mefenamic Acid from Ethyl-Cellulose Films in Isotonic Phosphate Buffer PH 6.8

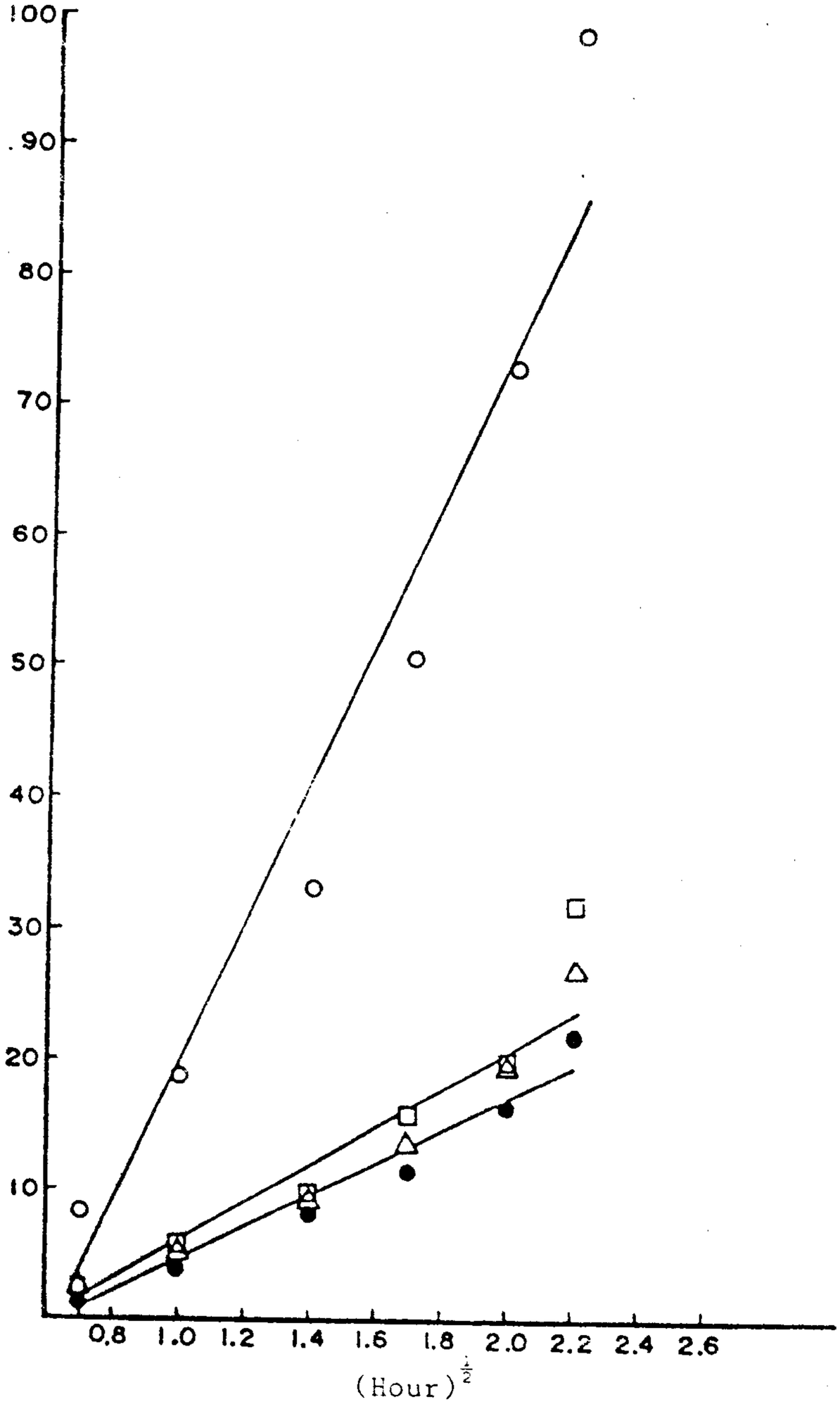

Fig. 6 : Release of Flufenamic Acid from Ethyl Cellulose Films in Isotonic Phosphate Buffer PH 6.8

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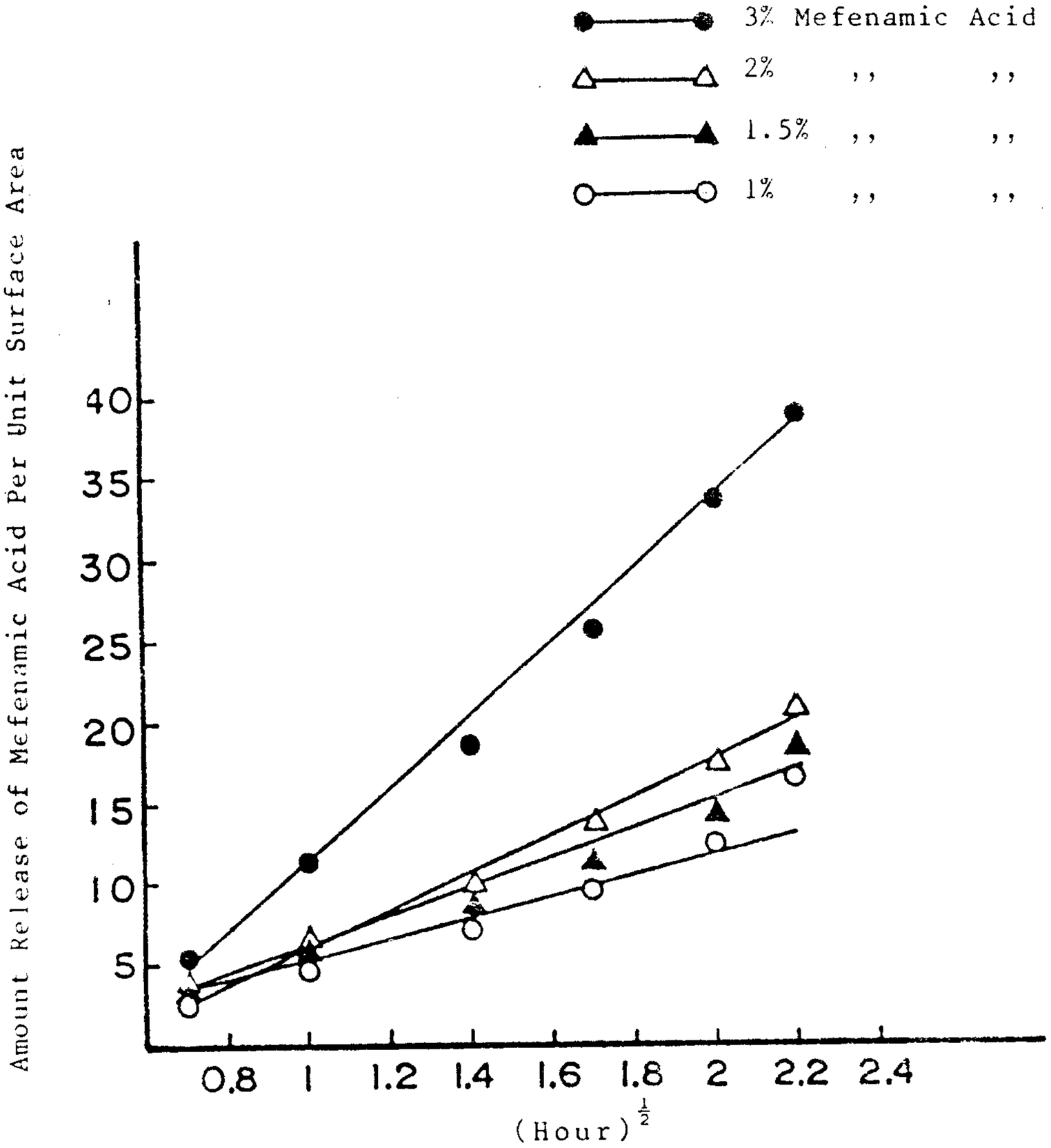

Fig. 7 : Release of Mefenamic Acid from Polyvinylacetate Film in Isotonic Phosphate Buffer PH 6.8

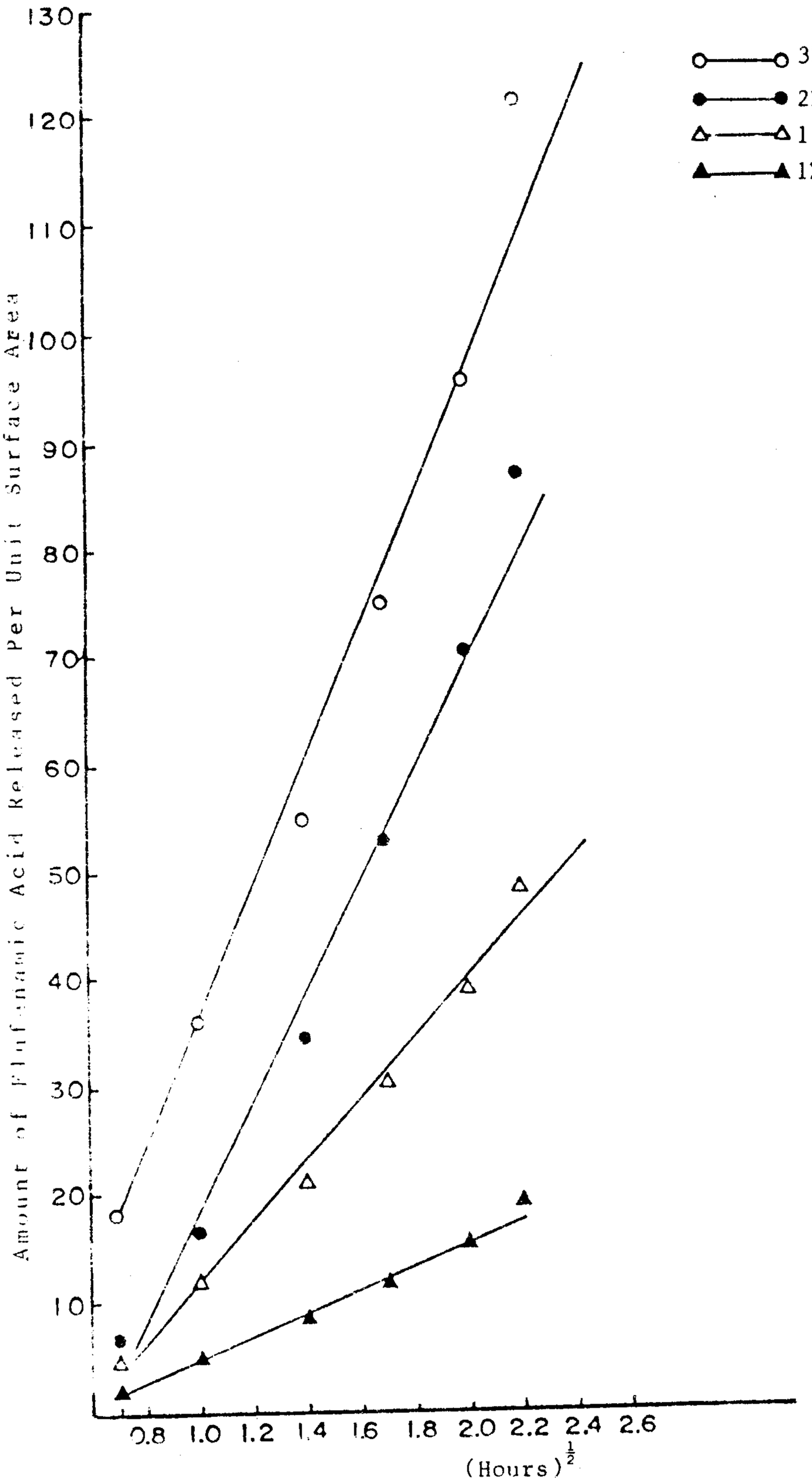

Fig. 8 : Release of Flufenamic Acid from Polyvinylacetate Films in Isotonic Phosphate Buffer Ph. 6.8

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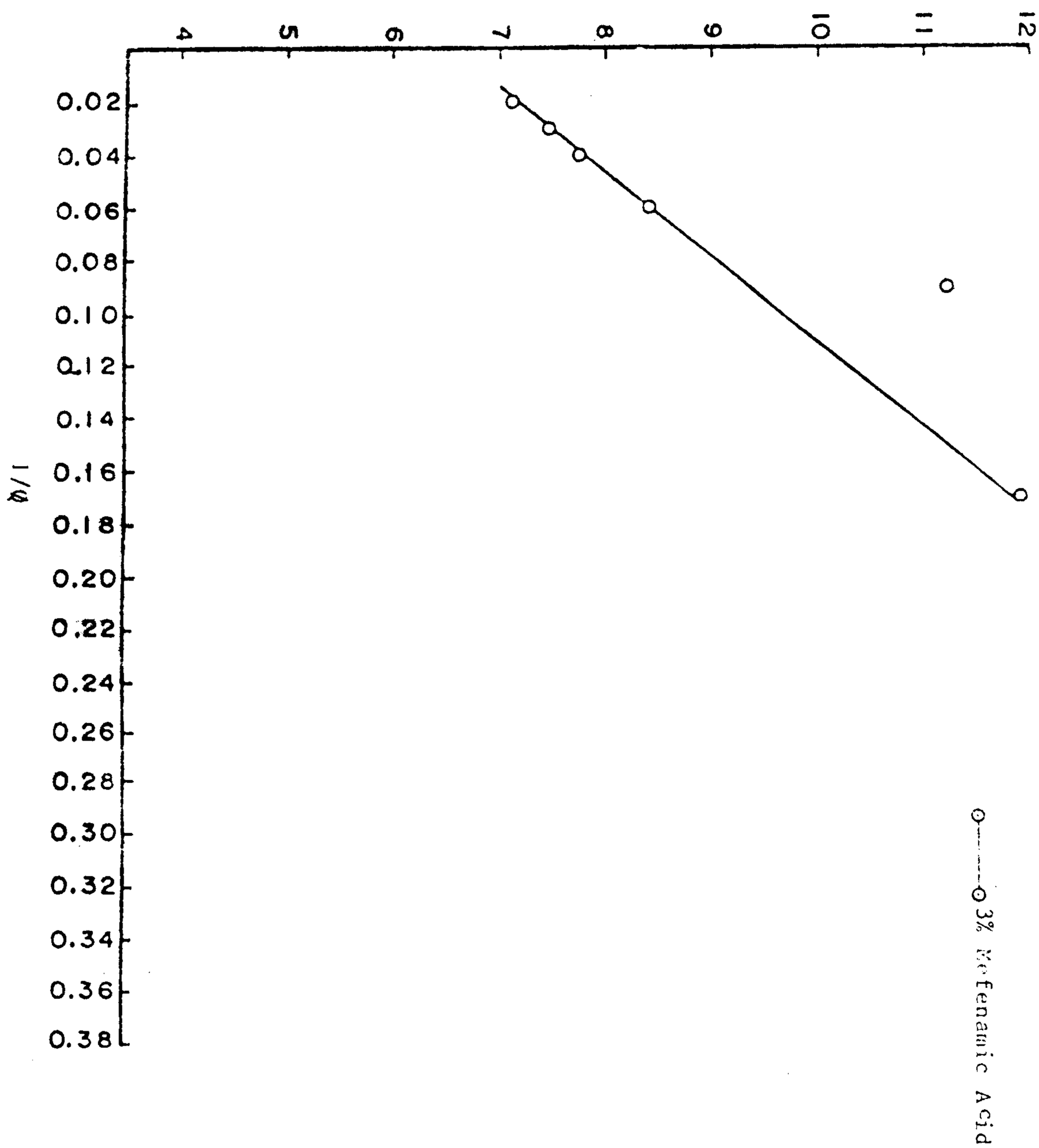

Fig 9: Plot of Released Rote Against Reciprocal of Amount of Drug. Released,

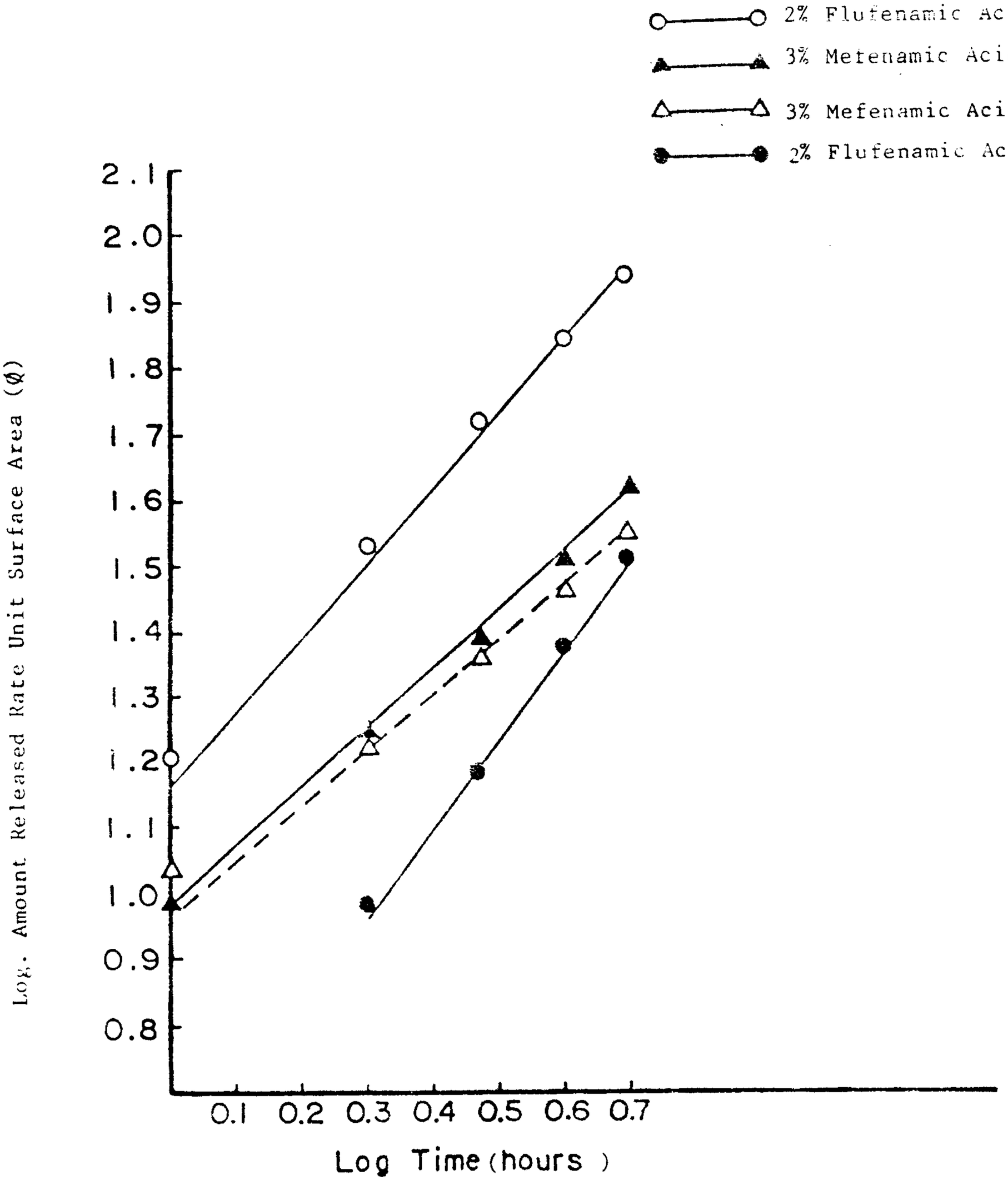

Fig. 10: Relationship of Log Ø̄ to Log t.(Release was Into Isotonic Phosphate Buffer pH 6.8).

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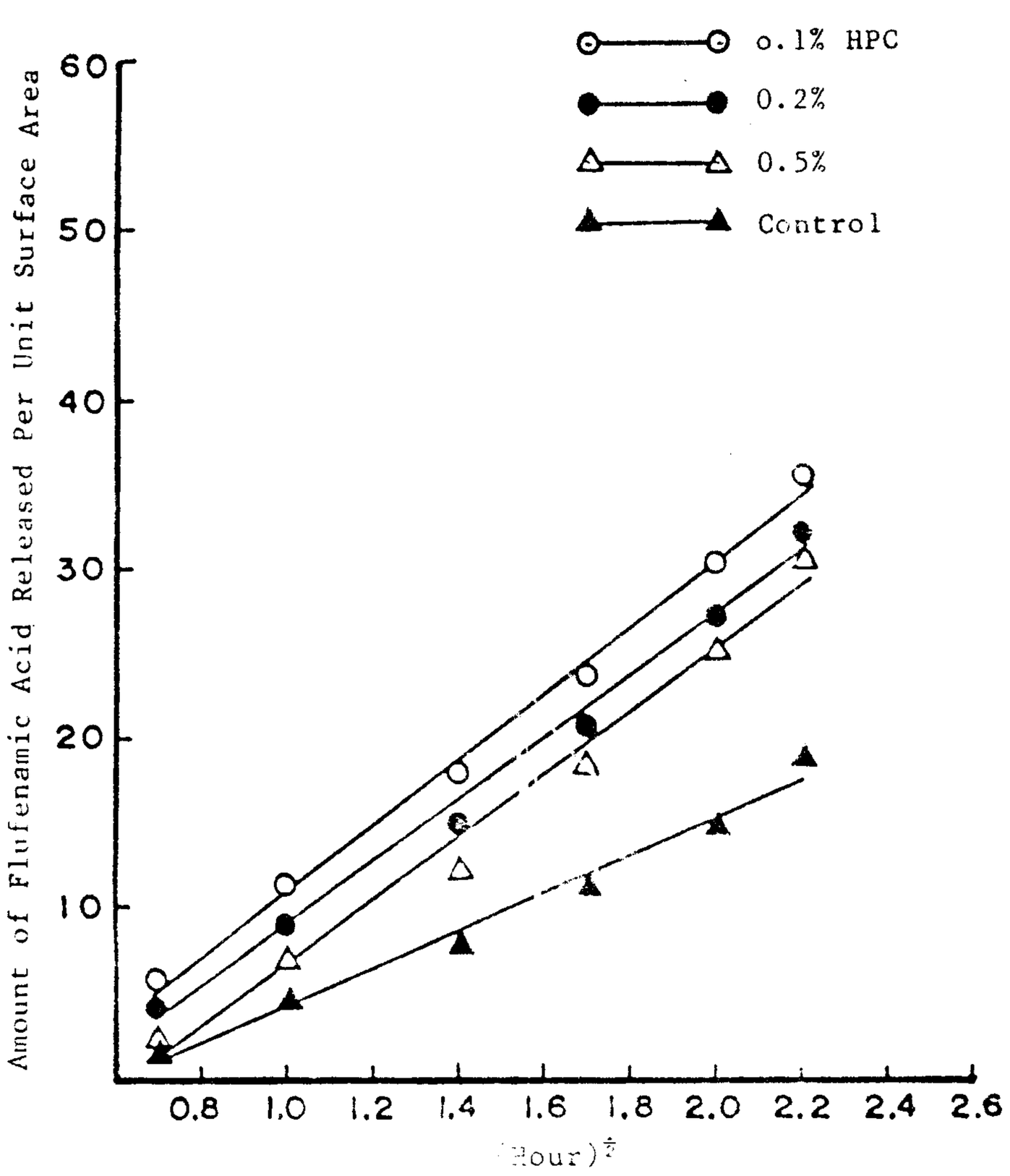

Fig. 11: Effect of Different Ratios of Hydroxypropyl Cellulose (HPC) on the Release of Flufenamic Acid from Polyvinylacetate Films.

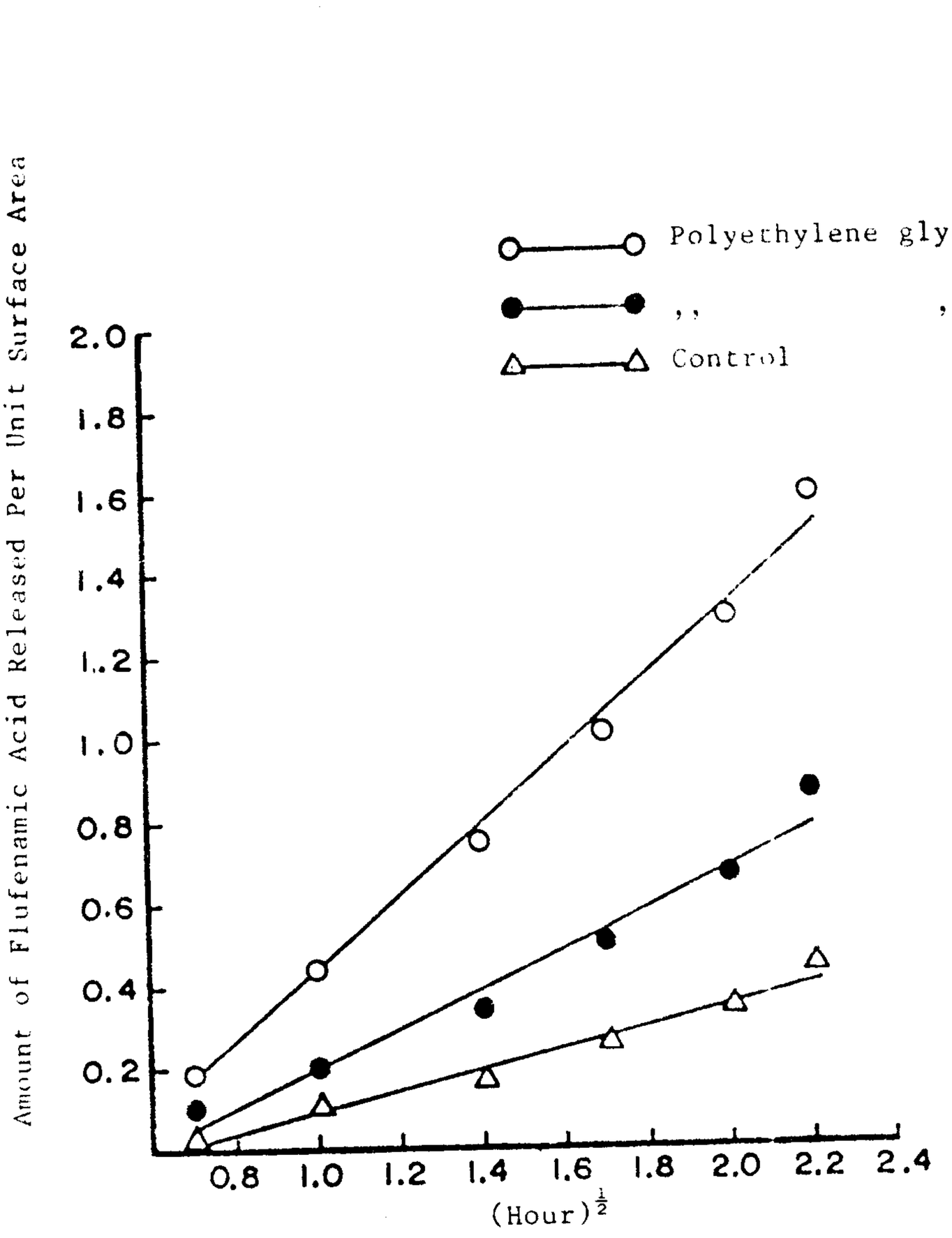

Fig. 12 : Effect of Polymer Additive on the Release of Flufenamic Acid from Ethyl Cellulose Films in Isotonic Phosphate Buffer PH 6.8

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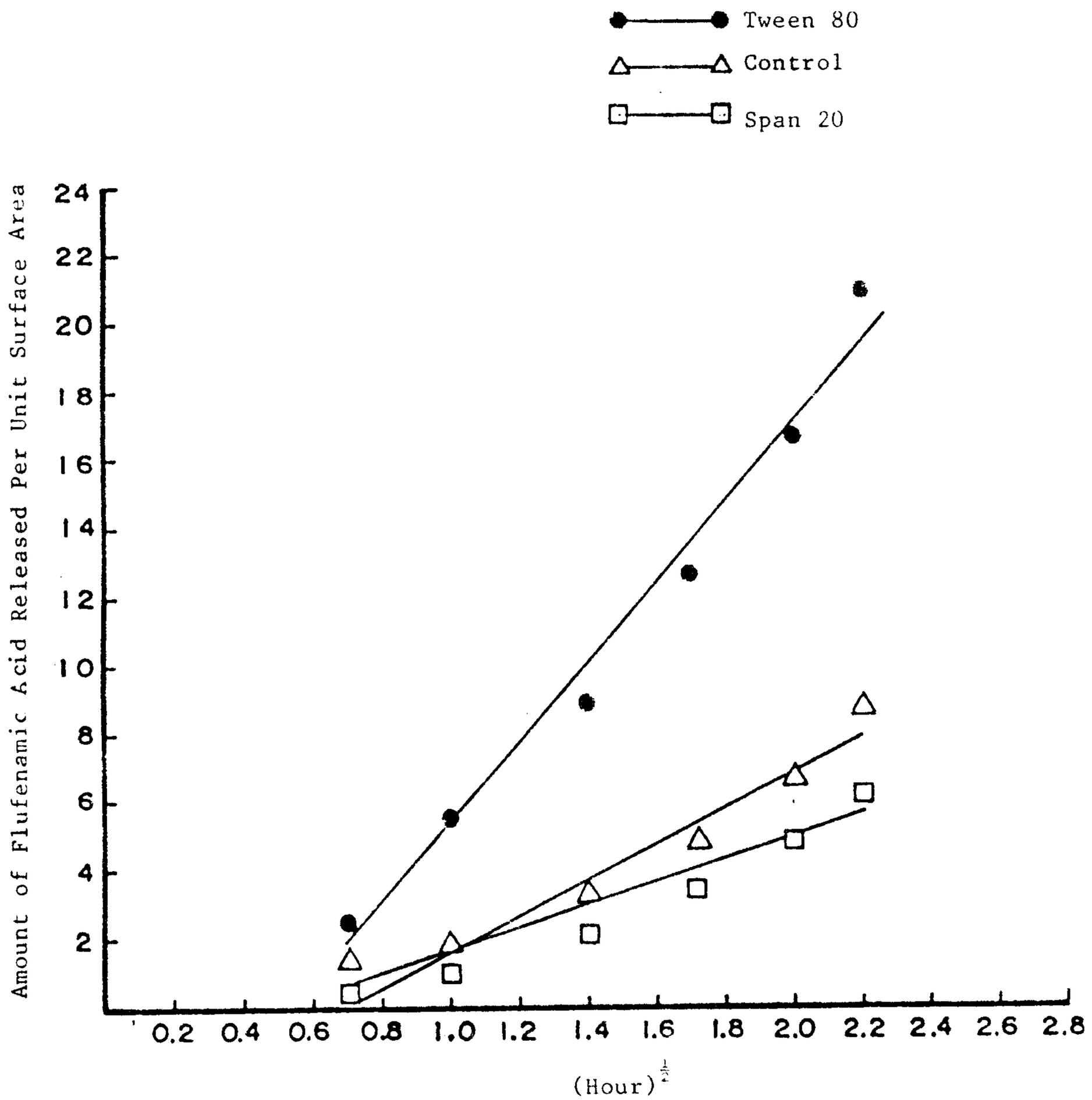

Fig. 13 : Effect of Surface Active Agents on the Release of Flufenamic Acid from Ethyl Cellulose Film In Isotonic Phosphate Buffer PH 6.8

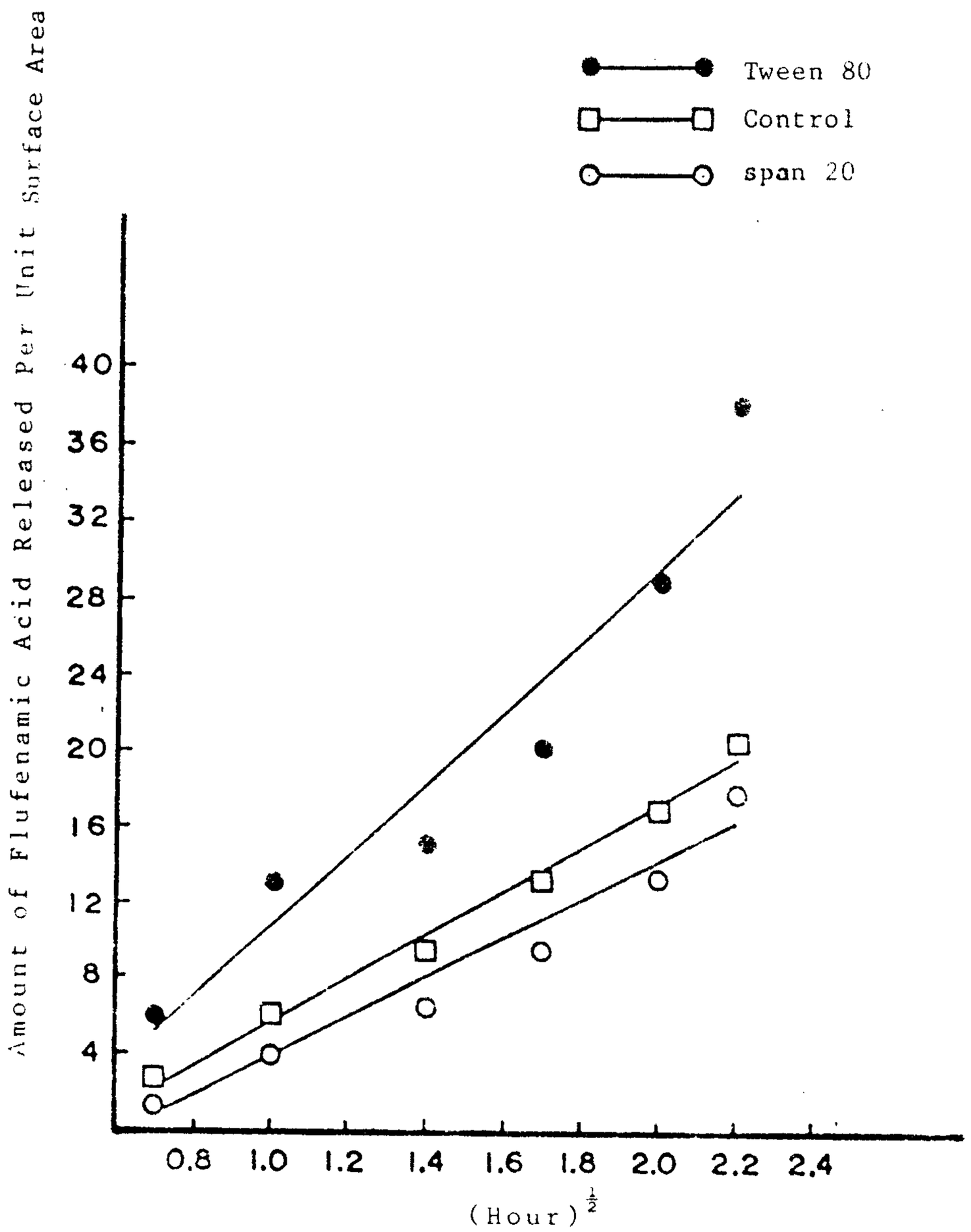

Fig.14 : Effect of Surface Active Agents on the Release of Mefenamic Acid from Ethyl Cellulose Film In Isotonic Phosphate Buffer PH 6.8.

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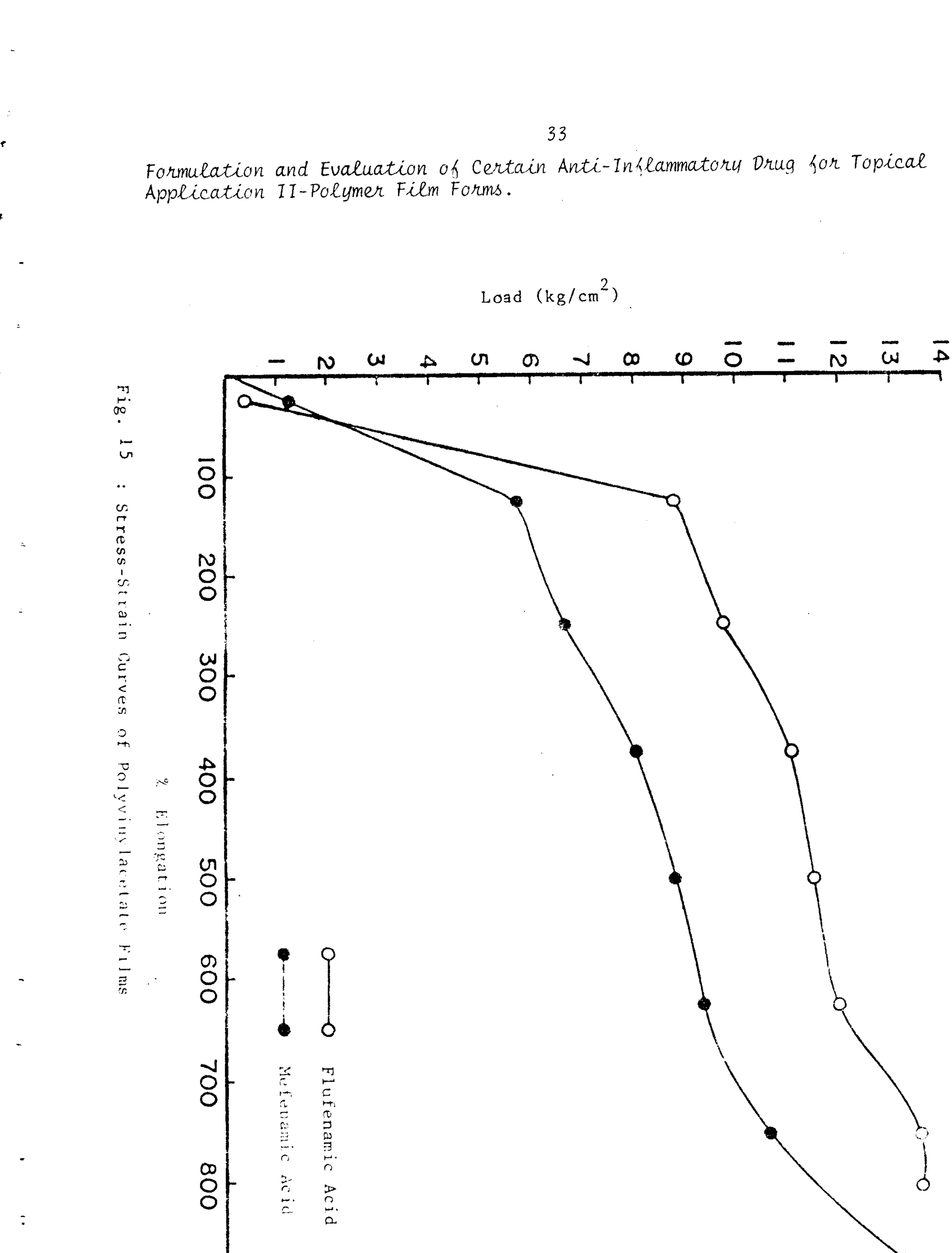

Fig. 15 : Stress-Strain Curves of Polyvinylacetate Films

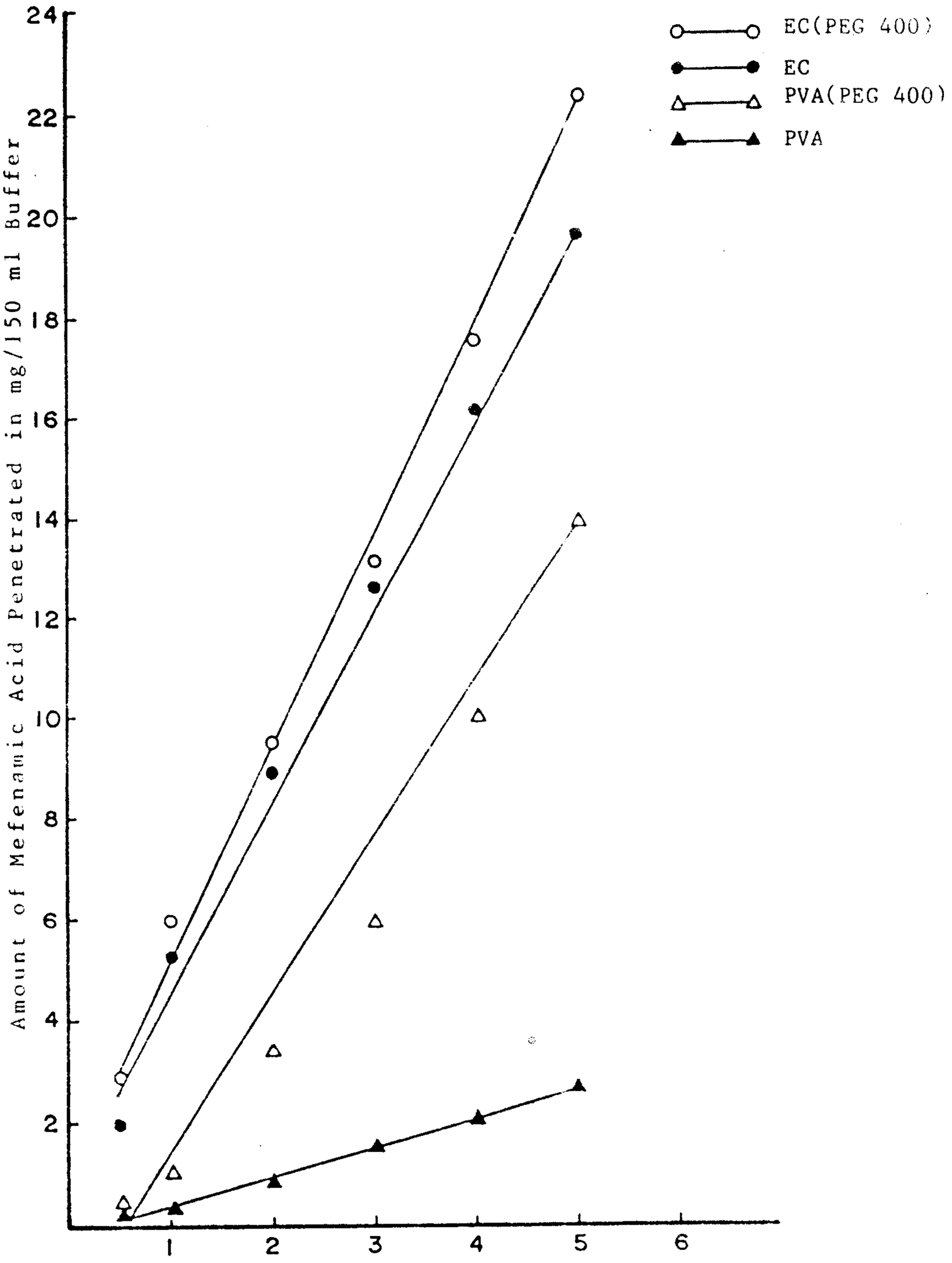

Fig. 16 : Effect of Polyethylene Glycol(PEG 400)on the Penetration of Mefenamic Acid Through Ethyl Cellulose(EC)and Polyvinylacetate(PVA) Films.

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تصميم وتقييم بعض الادوية المضادة للالتهابات للاستعمالات السطحية

٢ ـ رقائق البلمرات

سلوى صفوت ـ سهير الشنوانى ـ السيد على ابراهيم
قسم الصيدلانيات ـ كلية الصيدلة ـ جامعة أسيوط

فى هذا البحث تم دراسة ميكانيكية نفاذية كل من حامض الفلوفيناميك والميفيناميك فى الرقائق المكونة أساسا من نوعين من البلمرات وهى الايثيل سيليولوز وأسيتات البولى فينيل وعن طريق تعيين معدل نفاذية الدواء فى الغشاء وجد أن هناك علاقه طردية بين تركيز العقار فى الرقائق ومعدل النفاذية . وأشارت النتائج الى أن ميكانيكية النفاذية هى الانتشار وهى الميكانيكية الوحيدة التى يخضع لها كل من العقارين فى الرقائق .

كما أوضحت الدراسة أن تأثير الملدنات مثل بولى بروبيلين جليكول ٢٠٠٠ والبولى ايثيلين جليكول ٤٠٠ والمواد ذات النشاط السطحى مثل التوين ٨٠ يتوافق مع هذة الميكانيكية ويمكن تفسير ذلك بتأثير هذة المواد كمعدلات للذائبية وبالتالى تزيد هذة المركبات من معدل النفاذية .

وقد ثبت من الدراسة المعملية أن معدل نفاذية الدواء فى الرقائق يتزايد باضافة مواد ذات نشاط سطحى كمادة التوين ٨٠ أو جليكول بولى ايثيلين ٤٠٠ اوهيدروكسى بروبيل سيليولوز . كما وجد أن حامض الفلوفيناميك له معامل انتشار ومعامل نفاذية دائما أعلى من حامض الميفيناميك فى الرقائق المستعملة .

وكذلك تم دراسة خصائص النفاذية للادوية خلال الرقائق والعلاقة بين النفاذية من خلالها والنفاذية من جلد الفأر معمليا على أساس تعيين معامل النفاذية ومعامل الانتشار وقد اتضح من الدراسة أنه لاتوجد علاقه بين نفاذية كل من الدوائين من رقائق البلمرات والنفاذية خلال جلد الفأر .

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received in 26/12/1986 & accepted in 6/2/1987