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A CAST FILM APPROACH TO THE STUDY OF IN-VITRO DRUG RELEASE FROM OINTMENTS AND CREAMS

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ABSTRACT

The release rate of Nystation from a casted film of Amphocerin-E and Dehymuls-K ointment bases was investigated. The role of surfactants in enhancing the drug release was also studied. The rate of release of the drug from Dehymuls-K was found markedly higher than that of Amphocerin-E. The surfactants used markedly increase the release rate of the drug from the bases. Sodium lauryl sulfate, whether present in the casted film base or in the aqueous release medium enhances the rate of release of Nystation when compared to cetrimide. The effect of surfactant is more pronounced if it was added to the release medium than when incorporated in the casted base film. Higuchi model was applied for all experimental release data, where a good correlation was observed.

INTRODUCTION

The presence of dispersed particles in a matrix is a complex case found in pharmaceutical systems such as in drug release from inert matrices[1]. This may play an important role in percutaneous absorption especially when the solubility is very low[2,3]. Quantitative information

appears in the literature correlating drug release data with variation in physical parameters produced by compositional changes in the forulations[4,5]. Drug release may be altered by variation of the dimensional parameters of of the matrix, the matrix material, drug concentration in the film, film thickness and/or addition of surfactants[6,7].

The aim of this work was to study the factors and mechanisms controlling drug release from cast films.

The effect of base type and surfactants on the release of the drug from matrices in the form of casted film was investigated. Amphocerin-E, Dehymuls-K as commercial absorption bases, as well as cetrimide and sodium lauryl were used for this investigation. Nystatin was the drug of choice as an example of antifungal antibiotics.

EXPERIMENTAL

Materials:

Nystatin (British Drug House, Eng.), Amphoserin-E and Dehymuls-K (Dehydag products for Cosmetic Industry, Henkel International GmbH, Dusseldorf, West Cermany).

Procedure:

1-Preparation of matrix:

The base was melted on a water bath in an evaporating dish, then the calculated amount of the drug (20% Nystatin from the fraction that passed through sieve No.80 and retained on sieve No. 100 B.P.), was incorporated in the melted base. The mixture was allowed to coll to

room temperature while stirred. A specified weight (0.125 g.) of the prepared mass was transferred to a 250 ml capacity glass beaker with a cross-sectional area of 30 cm^2. The base was evenly distributed at the bottom with the aid of gentle heating on a water-bath, then allowed to cool immediately in a refrigerator in which it was kept overnight.

2-Release rate studies:

These were carried out by adding 75 ml of freshly prepared distilled water as a dissolution medium. The beakers were placed on an occillating shaker of 120 r.p.m., and covered with a plastic mount to prevent evaporation. Samples of one-ml were withdrawn at predetermined time intervals for spectrophotometric analysis at wave length 322 nm[8]. after filtration through millipore filter and futher dilution, using a double beam Pye-Unicum spectrophotometer (Model Sp 1800). The withdrawn samples were compansated by returning to the release media fresh samples of 1 ml at each time. The release experiment were carried out in triplicates. Blank expirements were performed by casting the films used (without the drug) and covering them with the media used in the experiment.

3-Incorporation of surfactants:

a-Surfactants in the matrix:

Cetrimide or sodium lauryl sulfate in concentrations of 0.05 and 1.0% were incorporated in the matrices. Plain base without surfactants was prepared for comparative study.

b-Surfactants in the release medium:

The release medium in this case was consisting of a solution of surfactant in a concentration of 0.001, 0.01 and 0.1%. A release medium free from surfactant was also used.

RESULTS AND DISCUSSION

Effect of Surfactants:

Fig. 1 Shows the effect of cetrimide and sodium lauryl sulfate incorporated in Amphocerin-E and Dehymuls-K on the release of Nystatin, while Fig. 2 shows the effect of both surfactants when present in the release medium.

It is obvious that the rate of drug release from Amphocerin-E is markedly less than that from Dehymuls-K in bases containing no surfactants. This may be due to the difference in the melting point of both bases (Dehymuls-K has a lower melting point than Ampocerin-E)[9]. The presence of surfactants, whether in the release medium or incorporated in the matrices, increases greatly the rate of Nystatin. This increase is proportional to the surfactant concentration and may be explained on the basis of the interpretation made by Duemling[10], that more rapid penetration of drugs is obtained by addition of wetting agents to the paraffin ointment. The author pointed out that surfactants have a great role in improving the character of topical vehicles, and also promoting the release of drugs from these bases. It is clear that the presence of sodium lauryl sulfate, whether mixed with Amphocerin-E base (Fig.1B) or present in the release medium (Fig.2) produced a markedly higher drug release than that with formulations with cetrimide. The same results were obtained in case of Dehymuls-K base (Fig.1D&2D).The increase of the release from Henkel bases (Amphoecrine-E, Dehymuls-K, Amphocerin-K, Edenox-K) of sparingly soluble drugs was prominent when using cetrimide rather than when using sodium la-

uryl sulphate. This may be due to the high penetrating power of the cationic surfactants and good wettability of these bases with this type of surfactants[9],(Fig 1C).

When the surfactant was present in the aqueous release medium, the rate of release of Nystatin from the two tested bases was much higher (Fig.2) than that obtained with the surfactant incorporated within the base itself (Fig.1). The continuous movement of the release medium containing surfactants on the top of the base film as a result of the shaking procedure, would leach out the drug from the upper surface of the film. This makes more channels available for the drug to diffuse to the external solution. The role of surfactant in increasing the solubility of the drug would be more clear and efficient as the drug becomes free and dissolves through the channels. It is worthwhile to mention that, in case of the presence of surfactants within the base, channels are also made available for drug release[11]. The effective porosity of the matrix would be increased as a result of channels made available for the drug to diffuse out to the external medium. The effect of surfactant present in aqueous release medium on potentiating the drug release from the base film may be related to the boundary layer being in direct contact with the solid solute via the porous matrix and consequent permeation through the matrix. Moreover, the shaking procedure, would renew this boundary layer bringing up a fresh part of surfactant solution close to the upper surface of the base film. This would increase the penetrative power for the surfactant and enhance its wettability effect.

The amount of drug released ,Q, was plotted versus the square root of time according to the Higuchi diffusion medel[12,13], Fig.3, where straight lines were obtained.

For further confirmation, the rate of drug released Q/t was plotted versus the quantily released Q, Fig 4 and 5 according to first order kinetics[13]. No linear relalionship was obtained, which indicates that the release of nyatain is not first order kinetics.

A Cast Film Approach to the Study of In-Vitro Drug Release from Ointments and Creams.

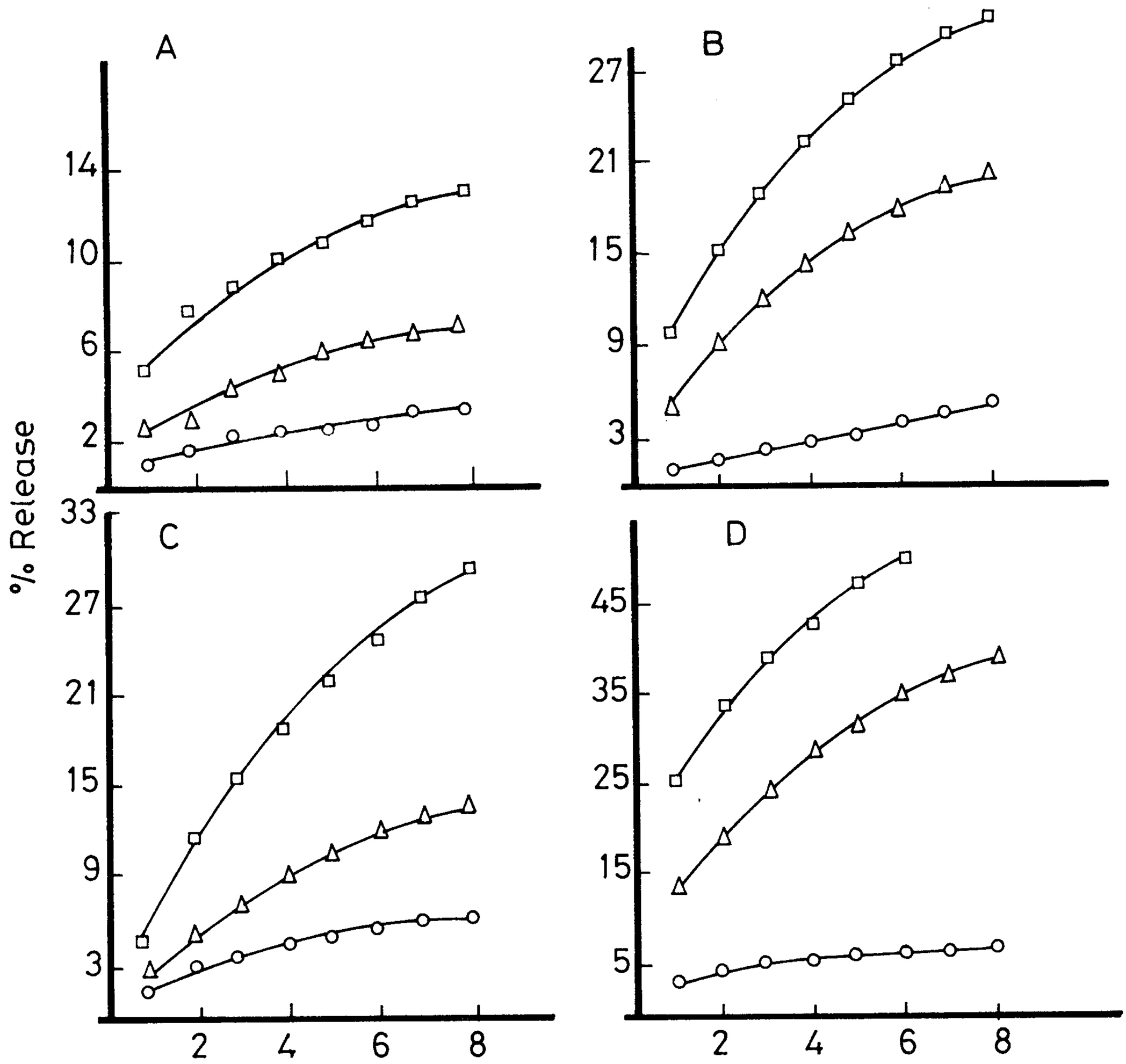

Figure 1: Effect of surfactant concentrations incorporated in the matrix, on the release of Nystatin

Key: Amphocerin-E incorporated with cetrimide(A) and sodium lauryl sulphate (B).

Dehymuls-K incorporated with cetrimide (C) and Sodium lauryl sulphate (D).

Surfactant concentrations: o 0%, Δ 0.5% and □ 1%.

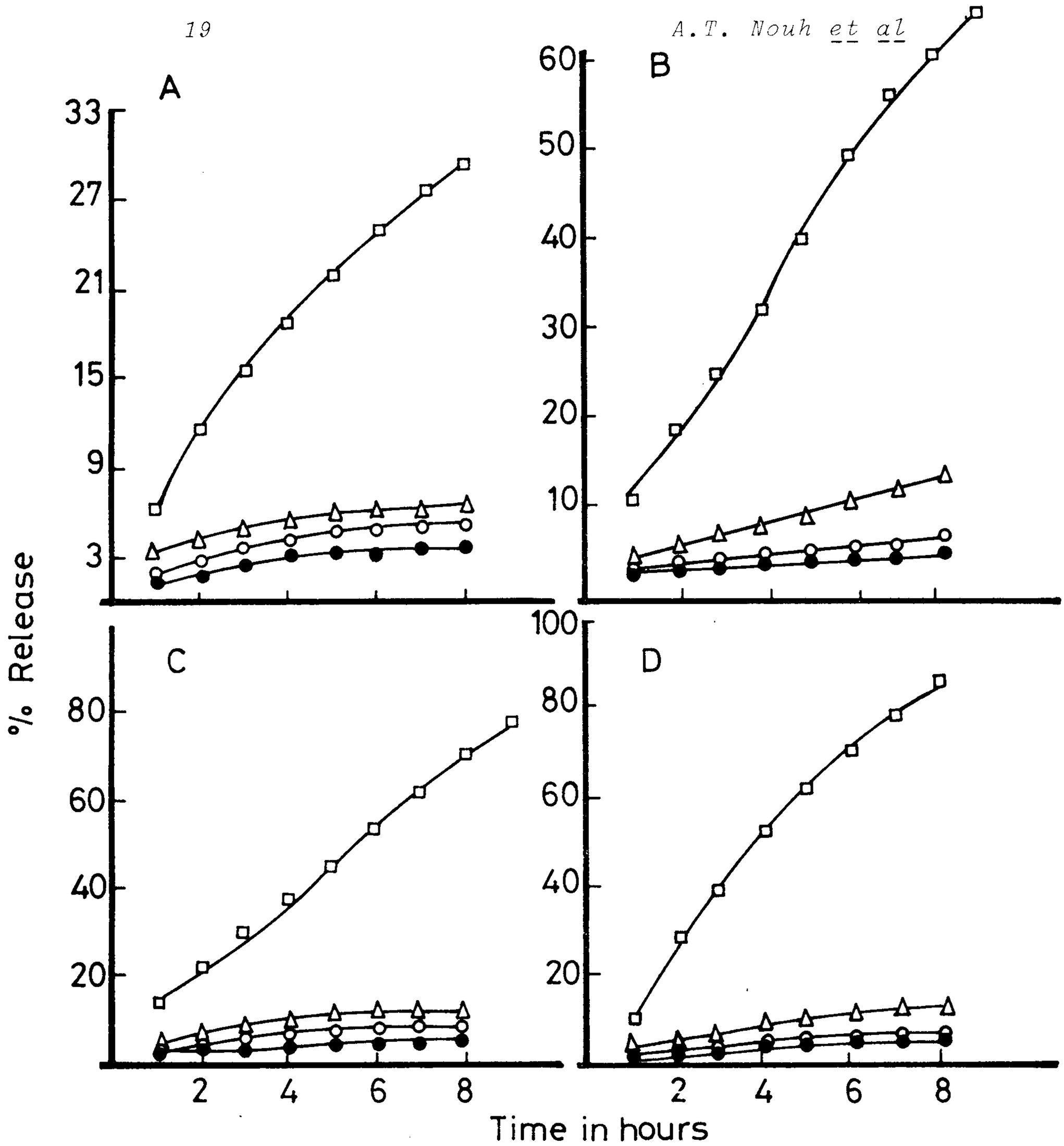

Figure 2 : Effect of surfactant concentrations present in the release medium on the release of Nystatin.

Key: Release medium containing cetrimide (A) and sodium lauryl sulphate (B) in case of Amphocerin-E.

Release medium containing cetrimide (C) and sodium lauryl sulphate (D) in case of Dehymuls-K.

Surfactant concentrations: ● 0 %, ○ 0.001%, △ 0.01% and □ 0.1%.

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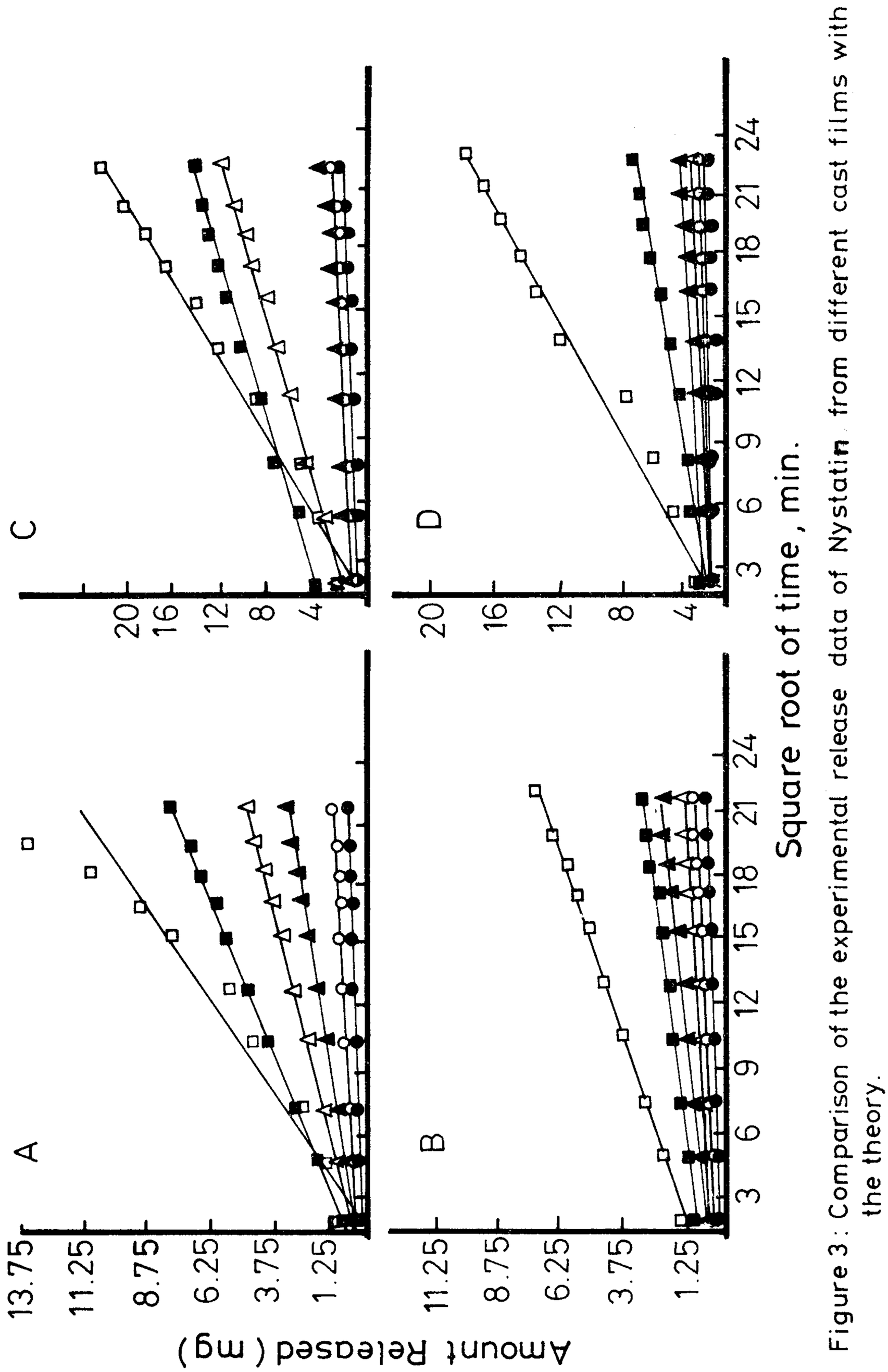

Figure 3: Comparison of the experimental release data of Nystatin from different cast films with the theory.
Ampocerin-E with sodium lauryl sulphate(A) and cetrimide(B).
Dehymuls-K with sodium lauryl sulphate (C) and cetrimide(D).
Surfactant concentrations: ● 0%, o 0.001, ▲ 0.01%, □ 0.1 %, Δ 0.5% and ■ 1.0 %

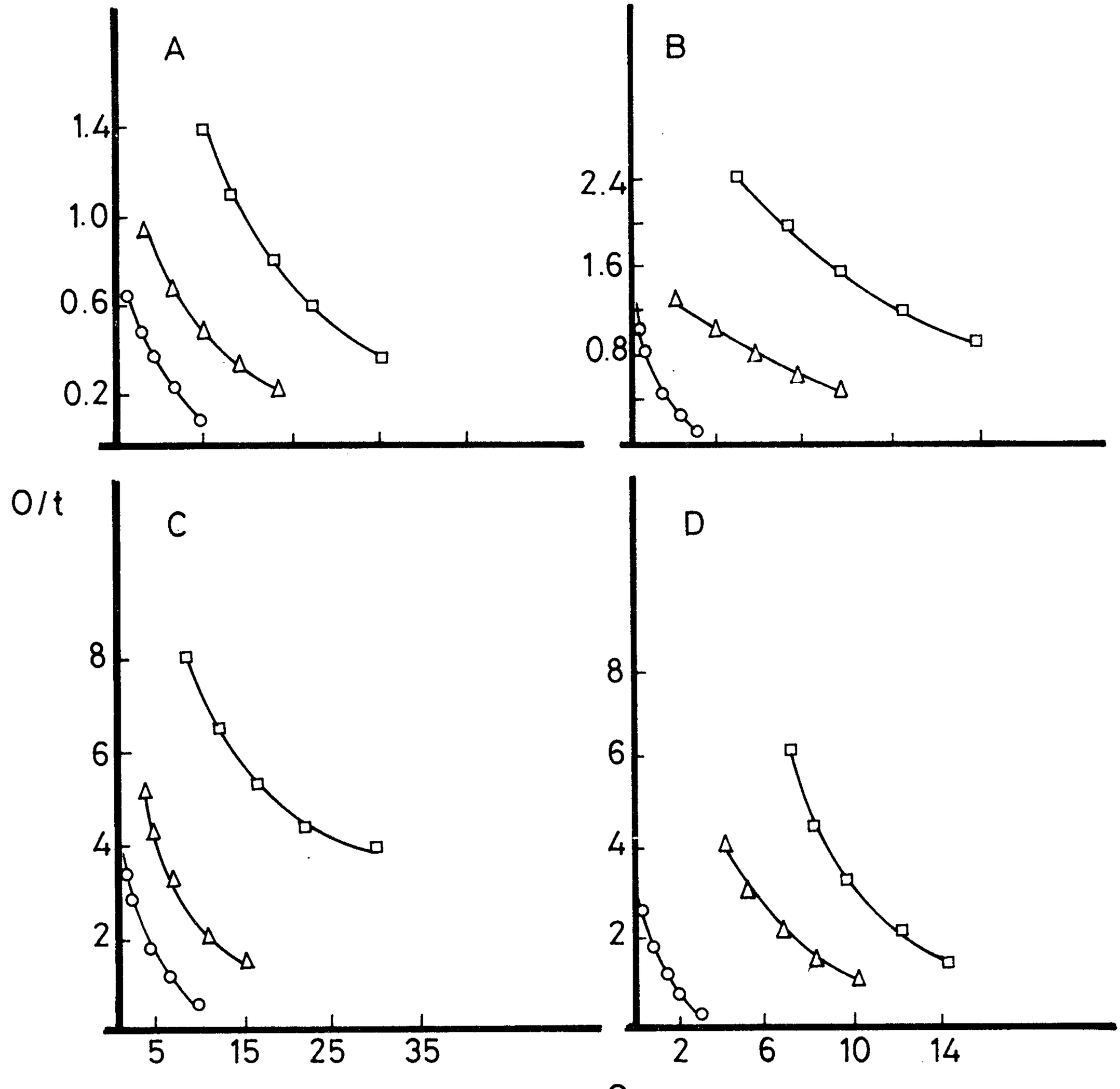

Figure 4: Relation between the release rate of Nystatin Q/t and amount released Q from Amphocerin-E and Dehymuls-K cast films.
Key: As in figure 1.

A Cast Film Approach to the Study of In-Vitro Drug Releast From Ointments and Creams.

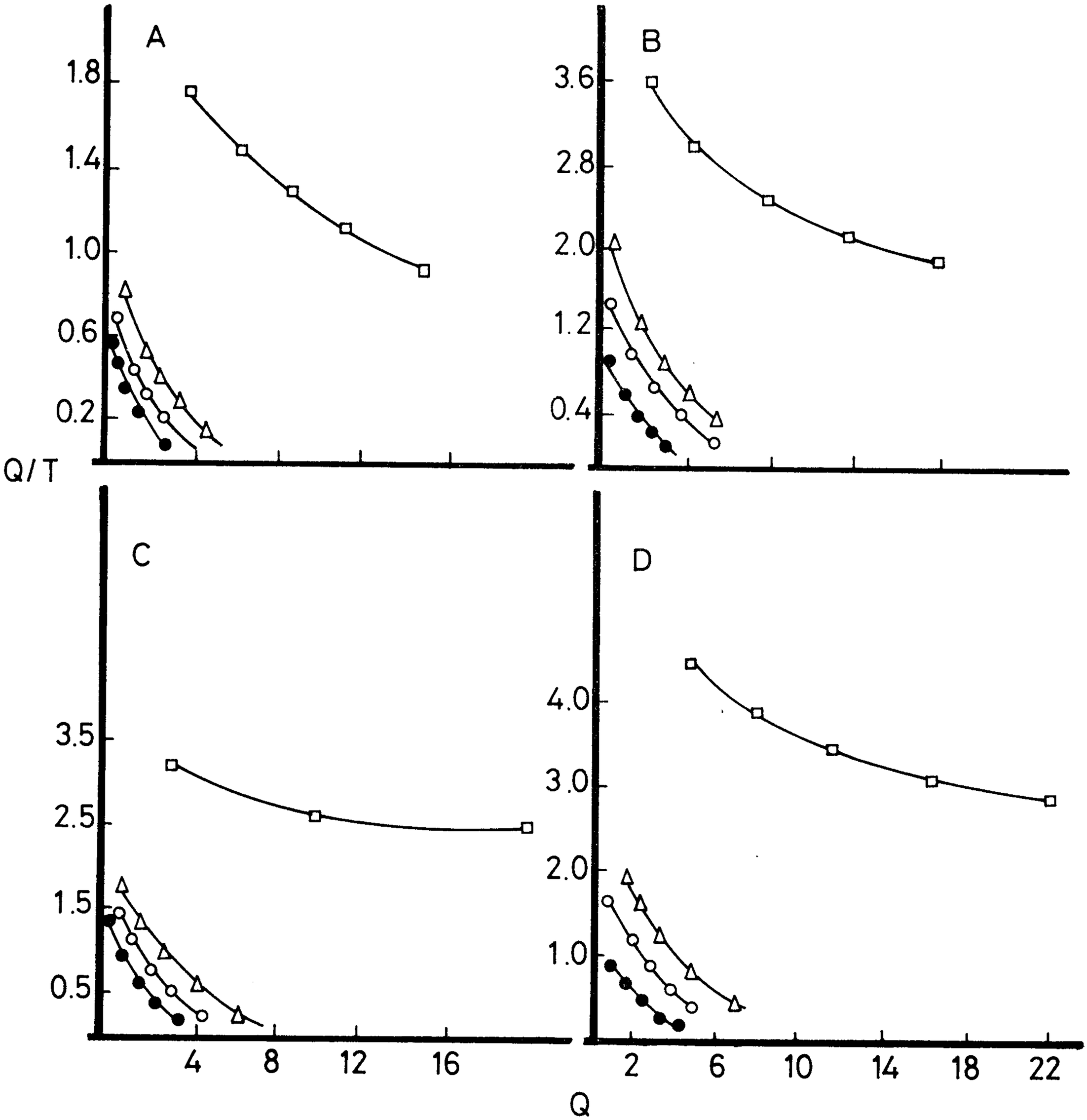

Figure 5: Relation between the release rate of Nystatin Q/t and amount released Q from Ampocerin-E and Dehymuls-K cast films.

Key: As in figure 2.

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دراسة على الخواص المميزة لانطلاق مادة النستاتين من الوسائد المصبوبة

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الغرض من هذه الدراسة هو ايجاد طريقة مناسبة لانطلاق الادوية من المراهم والكريمات ، ولقد استعملت مادتى الامفوسيرين ـ ه والديهيمولز ـ ك فى هذه الدراسة كقواعد تجارية وايضا مادة السيتريميد وكبريتات لاورات الصوديوم .

وبدراسة النتائج وجد ان كبريتات لاورات الصوديوم زادت من معدل انطلاق الدواء عن السيتريميد فى القواعد المستخدمة كما وجد ان انطلاق الدواء كان اكثر فى حالة استخدام الديهيمولز ـ ك عن الامفوسيرين فى وجود المواد ذوى النشاط السطحى وامكن ارجاع هذا الى درجة الانصهار المنخفضة نسبيا لمادة الديهيمولز ـ ك ولعوامل مختلفة اثناء تصنيع هذه القاعدة .

ووجد ان احتواء الوسط المائى للمواد المنشطة افضل من وجودها فى القاعدة نفسها على معدل انطلاق الدواء ـ ويرجع هذا للاتصال المباشر بين المادة النشطة سطحيا وبين سطح القاعدة مما ينتج عنه ثغور فى القاعدة تعمل كممرات للدواء الى الخارج .

هذا وقد امكن تطبيق نموذج هيجوشى على كل النتائج .

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