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EFFECT OF SURFACTANT STRUCTURE ON THE RELEASE OF DEXAMETHAZONE FROM DIFFERENT OINTMENT BASES

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The effect of variations in the surfactant molecular structure and concentration on the release of dexamethazone from different ointment bases, was investigated. It was found that the release of dexamethazone from oil in water emulsion bases increased in the presence of the different hydrophilic non-ionic surfactants used: This may be due to their solubilizing effect on such slightly water soluble solute. The increase in surfactant concentration enhanced the rate of drug released from each base by a special rate, specific for each base. The incorportion of hydrophobic surfactants in the water in oil emulsion bases leads also to increase in the amount of drug released. This may be due to the dispersing effect of these surfactants on such a drug.

Introduction

One of the most important functions of an ointment base is the control that it exerts on the release of medication which it carries [1]. For a drug to be effective it must be released first from the ointment base. Many investigators [2-3] studied the effect of surfactants on the release of drugs from ointment bases and other factors that may affect it.

Golucki [2], reported that the release of salicylic acid from petrolatum bases increased by the presence of surfactants. Other workers studied the effect of Tween 80 on the release of sulfathiazole from white petrolatum. It was found that the rate of drug release improved by increasing the surfactant concentrations [3]. On the other hand, others reported that the release of tetracycline hydrochloride from other ointment bases increased by the presence of non-ionic surfactants [4]. In some cases, it was found that while Tween 80 increased the rate of release of potassium iodide from emulsion bases, the presence of span 60 produced the opposite effect [5]. The purpose of this work is to study the effect of variations in the structure of non-ionic

surfactants on the release of dexamethazone from the various emulsion ointment bases as it may affect the availability of this drug from these bases.

Experimental

Materials :

Dexamenthazone[1].

Non-ionic surfactants, Emulgin C_{700} (Cetyl stearyl alcohol with 12 ethylene oxide units), Emulgin C_{1000} (Cetyl stearyl alcohol with 20 EO), Emulgin C_{1500} (Cetyl stearyl alcohol with 30 Eo) Emulgin 010 (Oleyl cetyl olcohol with 10 mol. EO), Emulgin 535 (Fatty alcohol polyglycol ether[2]. Brij 35 (Polyoxyethylene 23 lauryl ether), Brij 58 (Polyoxyethylene 20 cetyl ether), Brij 30 (Polyoxyethylene 10 cetyl ether[3], White soft paraffin, glycerin , stearyl alcohol[4].

The following formulations of the various ointment bases were prepared.

a) Water in oil emulsion base .

Dexamethazone	0.1 %
White soft paraffin	80 %
Non-ionic surfactant	18 %
Distilled water	12 %

b) Oil in water emulsion base

Dexamethazone	0.1 %
Stearyl alcohol	25 %
White soft paraffin	25 %
Glycerin	12 %
Non-ionic surfactant	5 %
Distilled water	33 %

(1) Sigma Chemicals, St., Louis, U.S.A.
(2) Henkel international, Dusseldorf, West Germany.
(3) Atlas chemical industries, Del. U.S.A.
(4) British drug houses, poole, England.

Methods

PREPARATION OF OINTMENTS

Four hydrophobic non-ionic surfactants were used for the preparation of various emulsion (w/o) ointment bases. These include Emulgin ^{C}700, Emulgin 010, Emulgin 535 as well as Brij 30.

Other ointment bases were also prepared using different concentrations (8,10 and 15%) of each surfactant. The hydrophobic non-ionic surfactants were used in different concentrations of (5, 7.5 and 10%) for the preparation of various O/W emulsion ointment bases. These surfactants were namely, Emulgin^{C}1000,Emulgin ^{C}1500, Brij 35 and Brij 58.

The release of dexamethazone was determined from each base seperately using the dialysis method[6]

The in-vitro release of dexamethazone from various ointment bases.

The ointment (I.g.) was accurately weighed and placed on a semipermeable fischer cellulose membrane[5] 30/32 to occupy a circle of 2 cm in diameter. The loaded membrane with the ointment was stretched over the open end of a glass tube 2 Cm in diameter which was made water tight by rubber band. The inverted tube was suspended so that the membrane was just below the surface of a predetermined quantity of 30 ml distilled water at 35 ± 2° contained in a 250 ml wide-mouth beaker. Samples each of 5 ml were withdrawn from the beaker at 15,30 minutes and 1,2,3,4,5 and 6 hours. They were assayed spectrophotometrically at 239[7] nm after appropiate dilutions, and an equal amount of water was returned to the beaker in order to maintain a constant volume.

RESULTS AND DISCUSSIONS

Water in oil emulsion bases:

It was noticed that the diffusion of dexamethazone increased from the bases containing hydrophobic non-ionic surfactants which Possess relatively lower HLB values. It was found that the base containing Emulgin ^{C}700 gave higher release than Emulgin 535,Figures 1 and 3.Furthermore the diffusion of dexamethaxone was inturn inhanced

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5- Fischer cellulose membrane London, U.K.

from the bases containing Brij 30 than Emulgin 010 as shown in Figures 2 and 4. The effect of surfactant on the release of dexamethazone from the various water in oil emulsion bases can be arranged in the following manner Emulgin C_{700} more than Emulgin 535 followed by Brij 30 and finally Emulgin 010. It was observed that the increase in concentration of non-ionic surfactant followed by an increase in the amount of drug diffused. This agreedwith the finding of Olszewski and kubis [3]. On the otherhand, the effect of the different concentrations of each non-ionic surfactant on the rate of diffusion did not occur with the same rate as shown in Figures 1-4. The increase in the release of such water insoluble drug from these ointment bases containing such hydrophobic surfactant can therefore be attributed due to their dispersing effect on such water insoluble drug.

Oil in water emulsion bases :

The release of dexamethazone from oil in water emulsion bases containing different types and concentrations of non-ionic surfactant was represented in Figures 5-8. It was observed that Emulgin C_{1000} gave the highest diffusion rate than Brij 35,and Brij58 as well as Emulgin C_{1500}. The three different concentrations of each non-ionic surfactant used were significantly increased the rate of release of dexamethazone from the various bases except in the case of Brij 35 and Brij 58. In the case of Brij 35 (Figure 7) there was no significant difference in the rate of diffusion between the two higher concentrations of non-ionic surfactant used (7.5% and 10% w/w) . This was also observed in the case of Brij 58 (5% w/w and 7.5% w/w) in comparison with the other surfactants as shown in - Figures 5-8. The increase in the release of such water insoluble drug from these ointment bases containing such hydrophilic surfactant used (7.5 and 10% /w) . This was also observed in the case

of Brij 58 (5% w/w) and 7.5% w w in comparison with the other surfactants as shown in Figures 5 - 8. The increase in the release of such water insoluble drug from these ointment bases containing such hydrophilic surfactants may be due to their solubilizing effect on such a drug. This agreed with other workers[3], finding on the release of slightly water soluble drugs from other ointment bases. Although the effect of surfactant on viscosity of tne base may play a part together with some other factors this will be the scope of further study which will be reported latter on.

From the previous results it can be concluded that the rate of diffusion of dexamethazone was mainly affected by the type and concentration of the surfactant used. In oil in water emulsion base, the hydrophilic non-ionic surfactants employed possess relatively high HLB values. It was found that Emulgin^{C}1000 gave higher diffusion rate than Emulgin ^{C}1500, which can be attributed as follows. Emulgin^{C}1500 possess a larger ethylene oxide chain than Emulgin^{C}1000 but for the same hydrocarbon chain length. Therfore the relative volume of the hydrocarbon part of the micelle to the total micellar volume, shoud be less for Emulgin^{C}1500 than Emulgin^{C}1000 surfactants micelles. Consequently the solubilizing power of Emulgin^{C}1500 micelles was expected to be less than Emulgin^{C}1000 for such water insoluble solute. It can be concluded that these non-ionic surfactants may enhance the rate of diffusion of dexamethazone from these O/W emulsion bases mainly due to their solubilizing effect. The same interpretation can be also applied in the case of Brij 35 and Brij 58 but in the case of Brij 58 the volume of the hydrocarbon core of the micelles was much higher than Brij 35 for the same ethylene oxide part of the micelles and this can explain why the incroporation of the first in the oil in water emulsion bases gave better release value than the letter. This also indicates that the core of the micelle is the main site for the incorporation of this drug and that the core volume can affect greatly their solvent power and therefore the release of this solute especially from O/W emulsion bases.

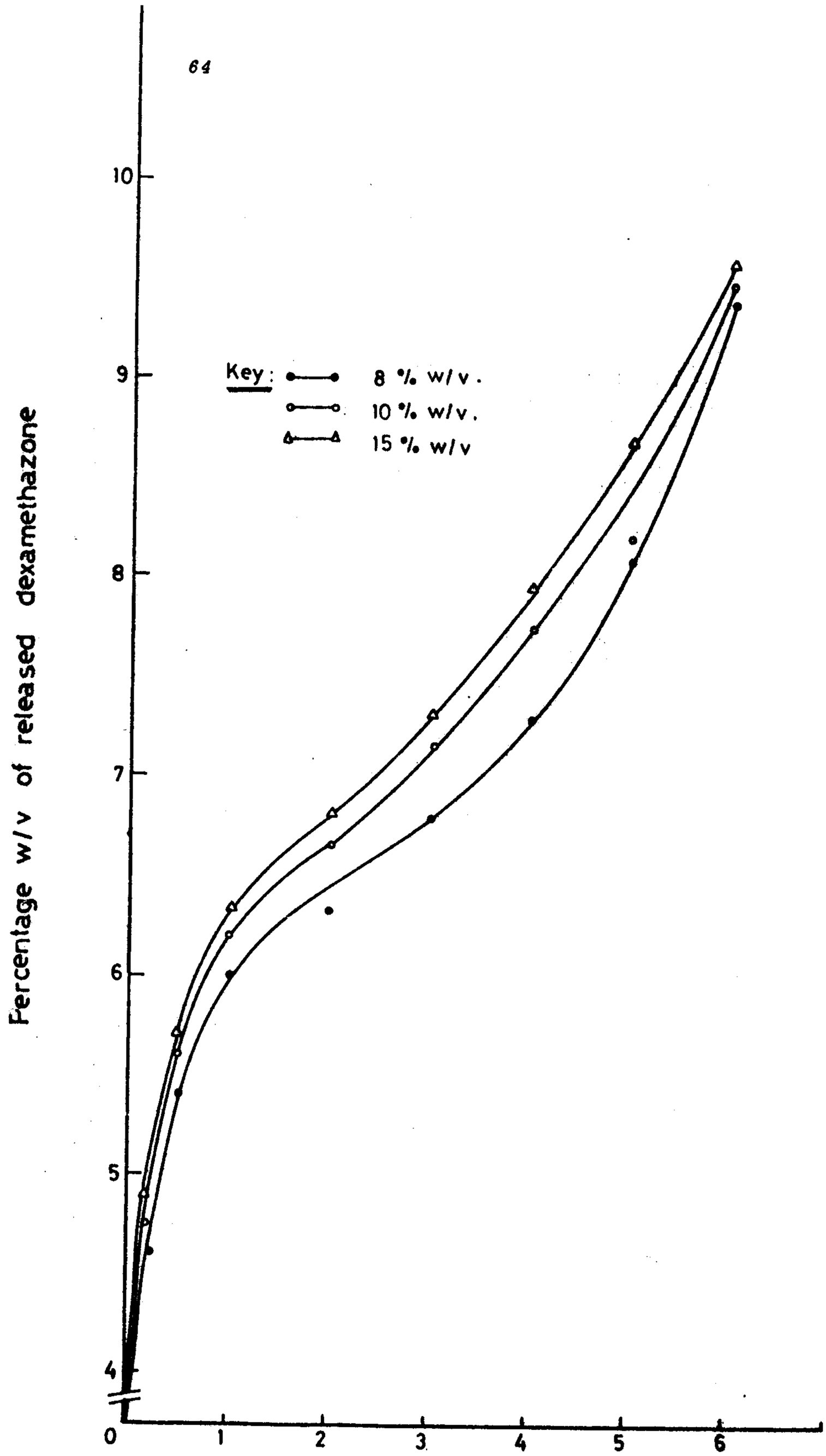

Fig.(1) Release of dexamethazone from water in oil emulsion base containing different concentrations of Emulgin C_{700}.

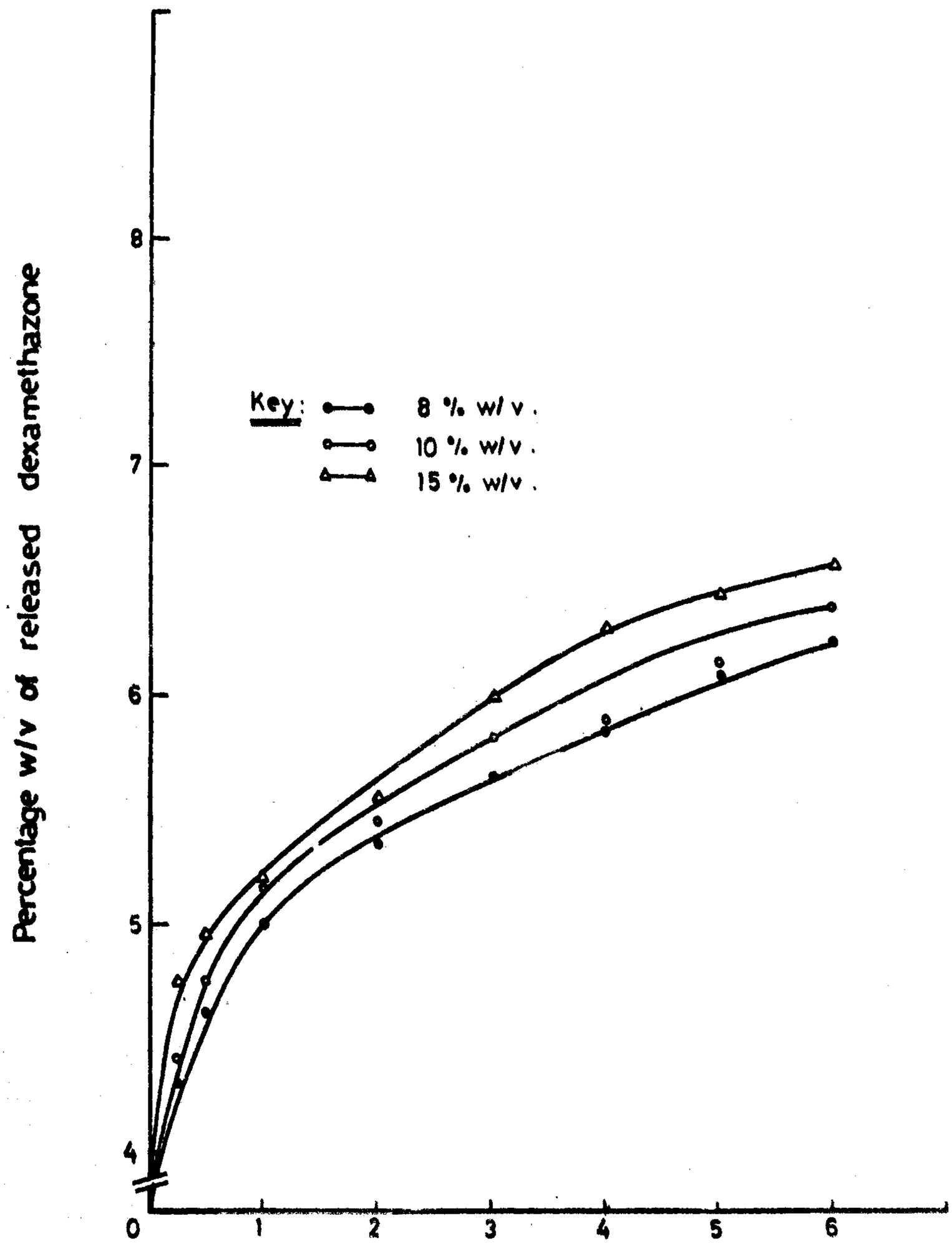

Fig.(2) Release of dexamethazone from water in oil emulsion base containing different concentrations of Emulgin 010.

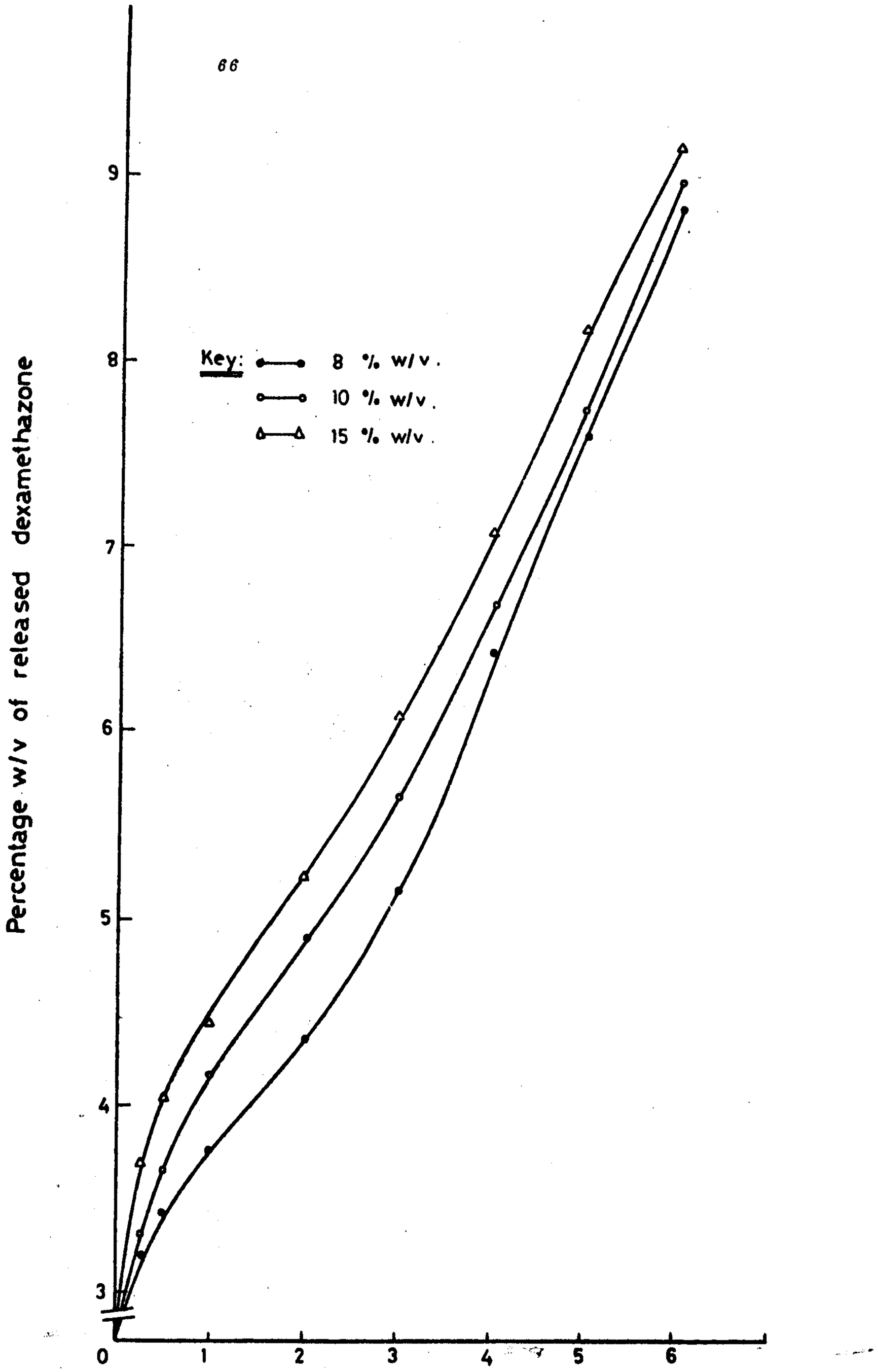

Fig.(3) Release of dexamethazone from water in oil emulsion base containing different concentrations of Emulgin 535.

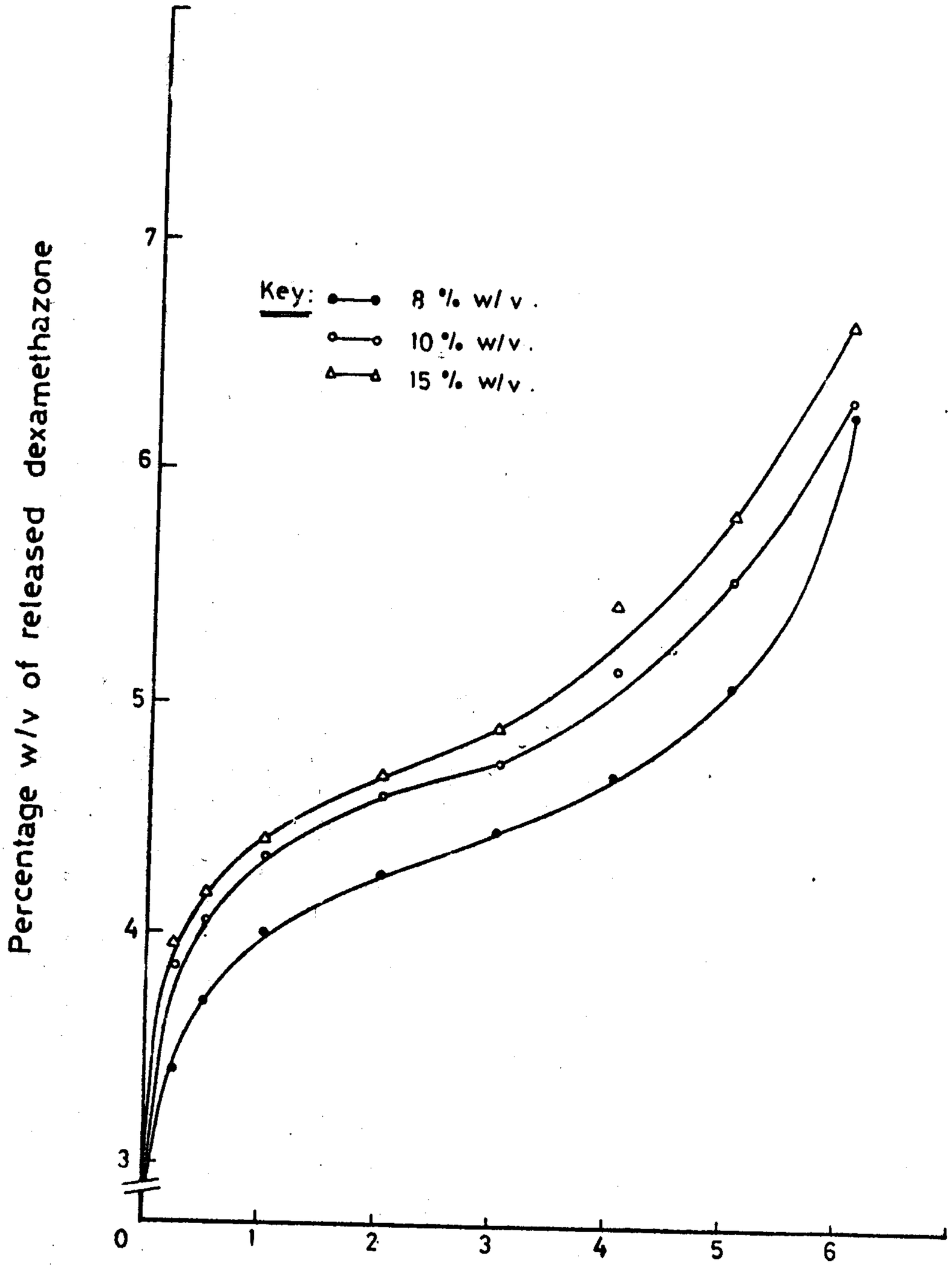

Fig.(4) Release of dexamethazone from water in oil emulsion base containing different concentrations of Brij 30.

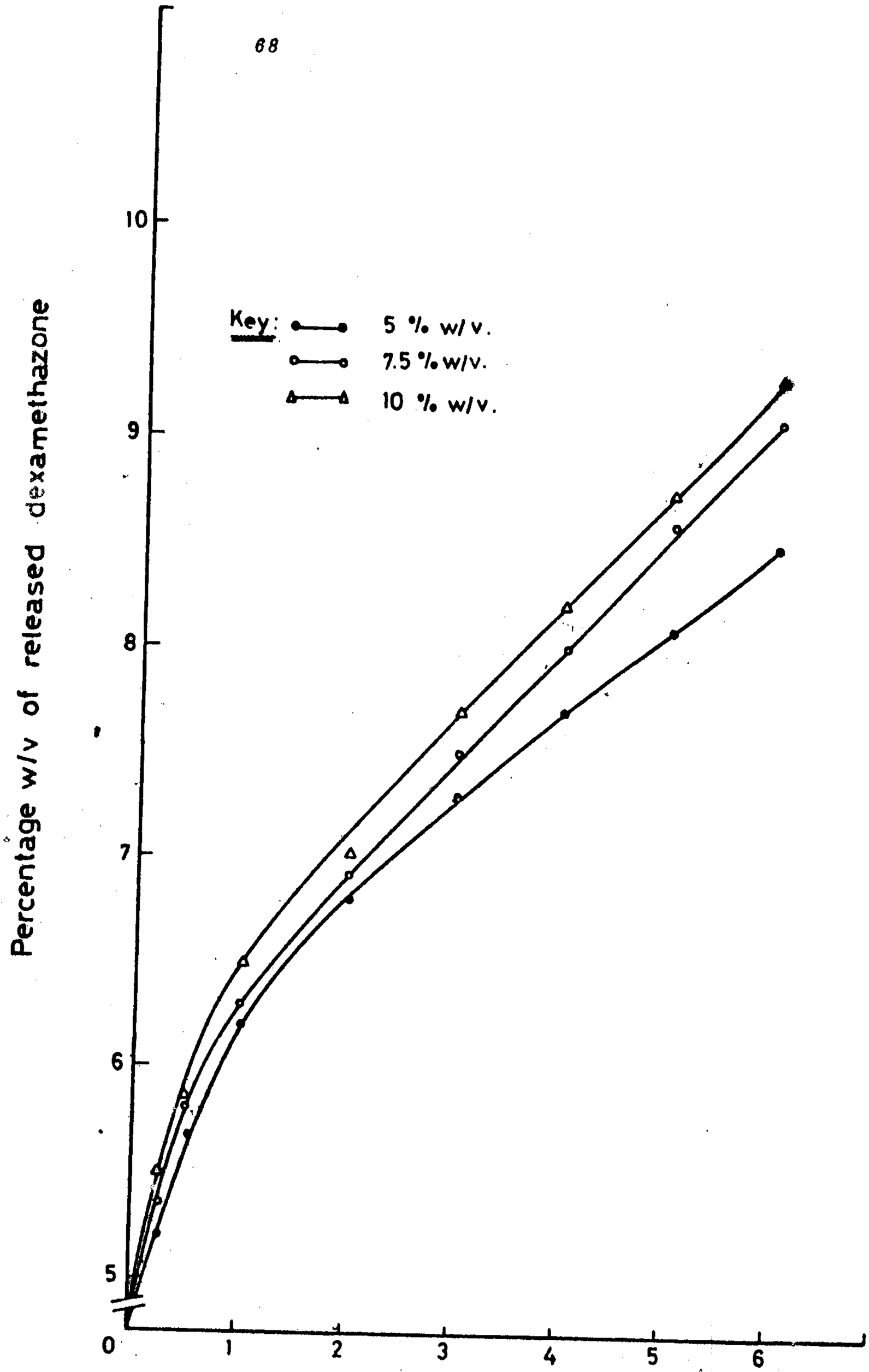

Fig.(5) Release of dexamethazone from oil in water emulsion base containing different concentrations of Emulgin C_{1000}.

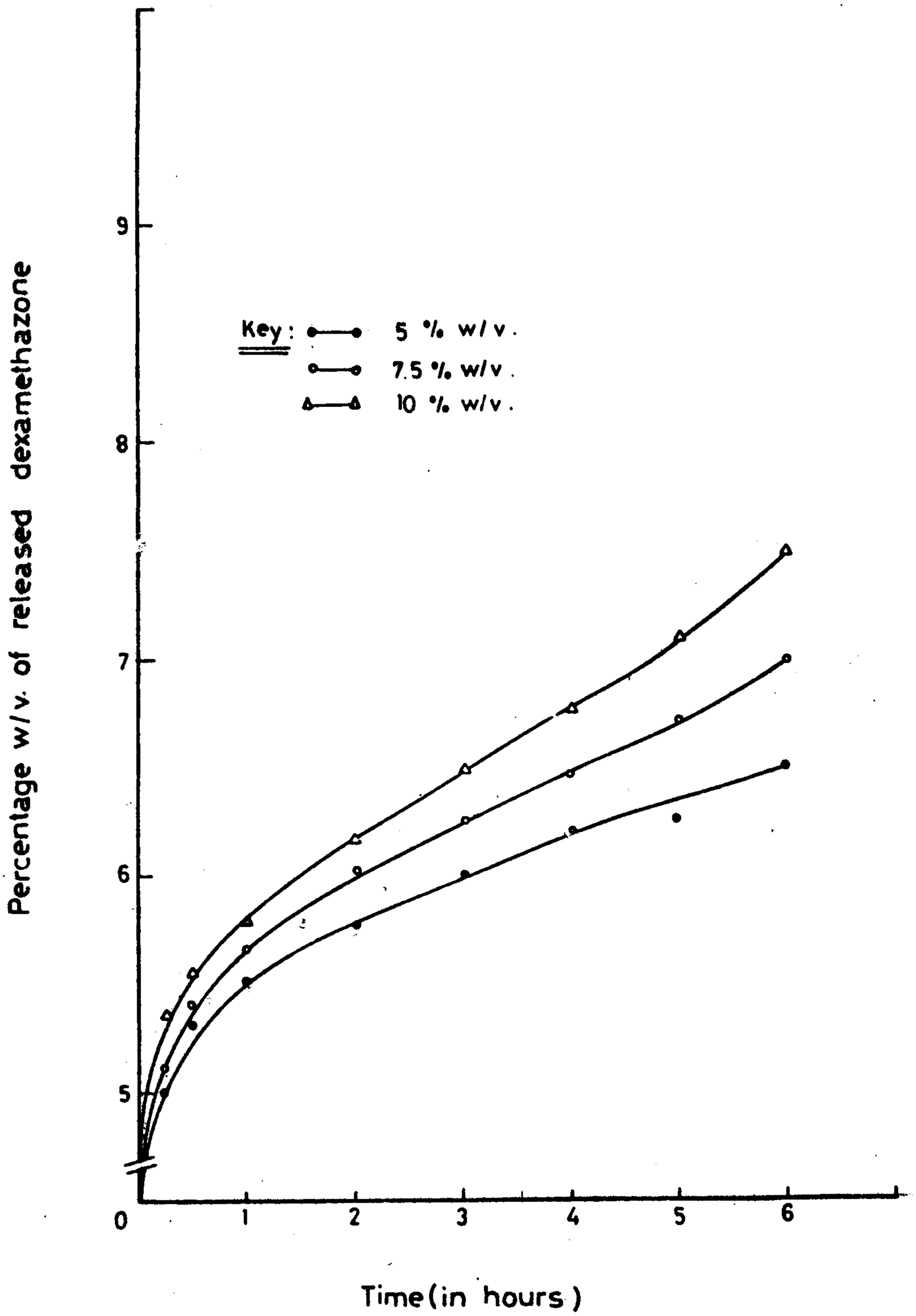

Fig.(6) Release of dexamethazone from oil in water emulsion base containing different concentrations of Emulgin C_{1500}.

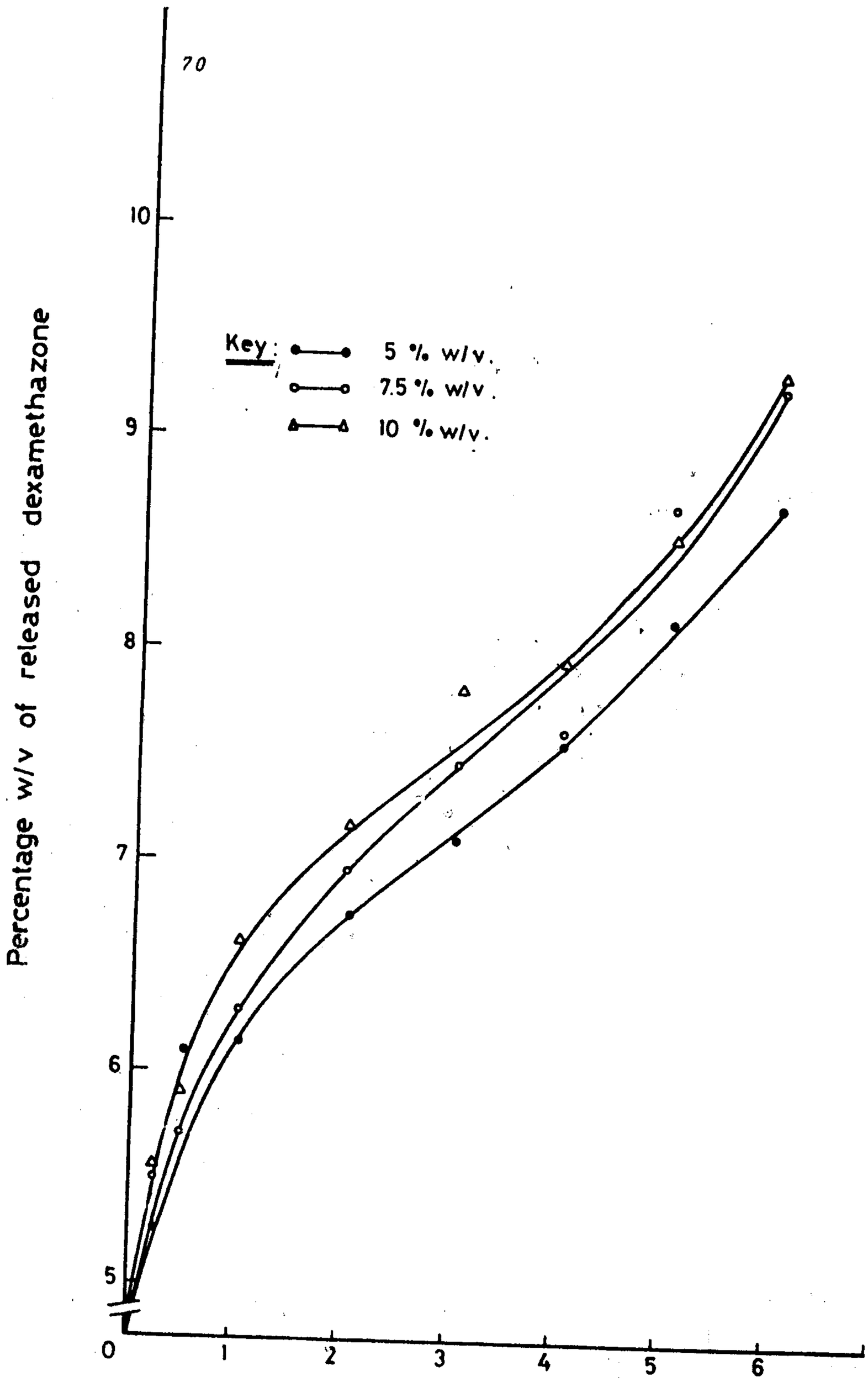

Fig.(7) Release of dexamethazone from oil in water emulsion base containing different concentrations of Brij 35.

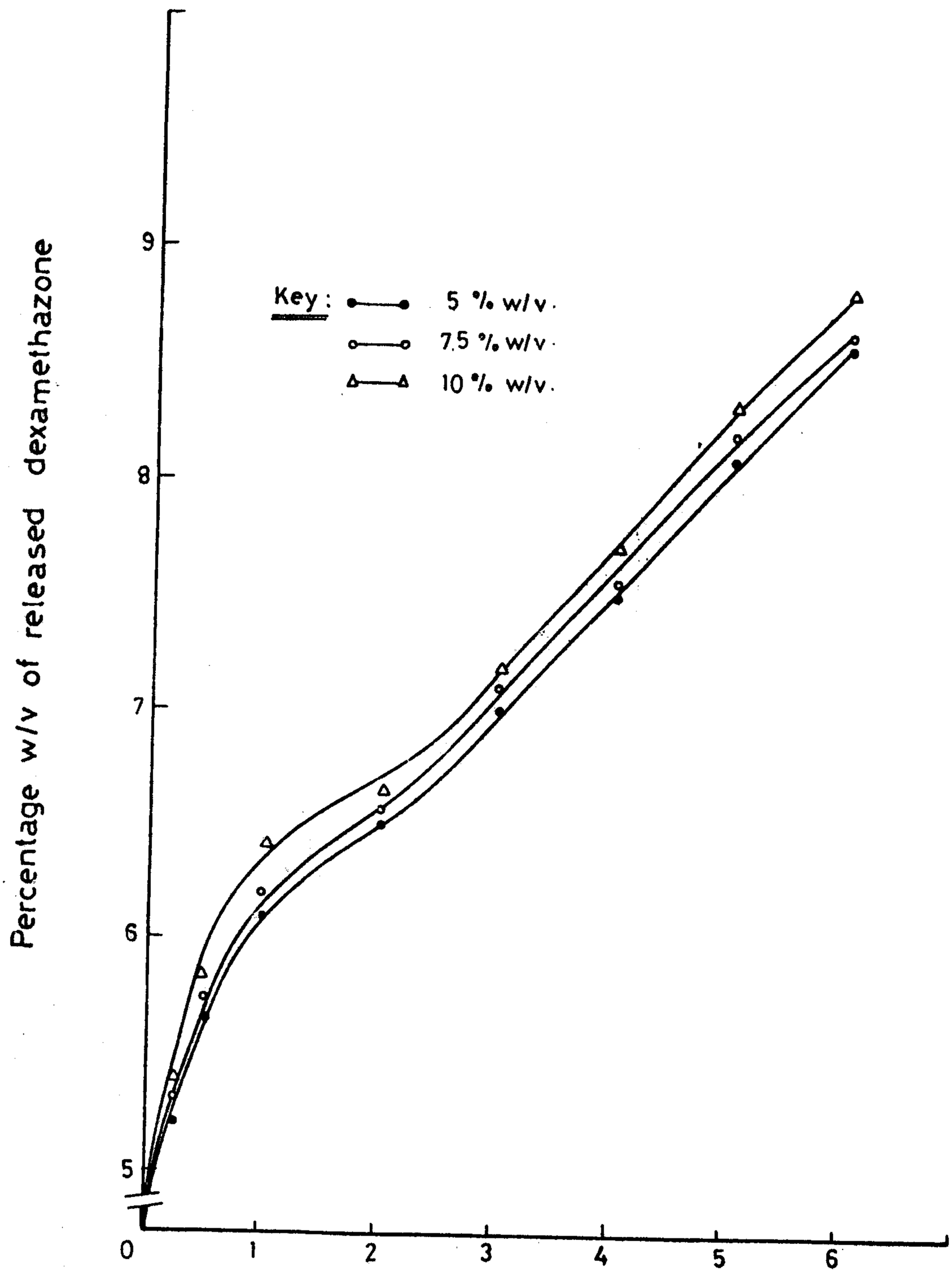

Fig.(8) Release of dexamethazone from oil in water emulsion base containing different concentrations of Brij 58.

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تأثير التركيب الجزيئي للمنشطات السطحية على اتاحة الدكساميثازون من قواعد المراهم المختلفة

فوزية سيد حبيب ـ احمد السيد ابوطالب ـ محمد على عطيه
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تم دراسة تأثير التغييرات فى التركيبات الجزئية وكذلك التركيزات المختلفة للمنشطات السطحية على درجة اتاحة الدكساميثازون من قواعد المراهم المختلفة.

وقد وجد ان درجة اتاحة الدكساميثازون تزيد فى وجود المنشطات السطحية الغير متأينة المحبة للماء وذلك من القواعد التى تحتوى على ماء زيت.

ويعلل ذلك نتيجة لزيادة درجة الذوبان لهذه المادة شحيحه الذوبان وقد وجد ان زيادة تركيز المنشط السطحى يزيد من درجة الاتاحة من كل قاعدة على حدة بنسبة مختلفة .

وقد ثبت انه عند اضافة المنشطات السطحية المحبة للزيت للقواعد التى تحتوى على ماء زيت يزيد ايضا من درجة اتاحة الدكساميثازون ويعلل ذلك نتيجة لتأثير المنشط السطحى على زيادة انتشار هذا العقار.