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DISSOLUTION STUDY ON SULPHAPYRIDINE, AND SULPHISOXAZOLE FROM THEIR SOLID DISPERSIONS AND COPRECIPITATES

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The dissolution behaviour of sulphapyridine, sulphamerazine and sulphisoxazole was investigated from their solid dispersions using PEG 4000, 6000 and coprecipitates using PvP 25, 000. It was found that the rate of dissolution was much greater from the preparations containing solid dispersions as well as coprecipitates for the three sulphonamides investigated. The polymer to drug ratio and the molecular stracture, as well as the nature of the polymer may also affect the rate of release of each sulphonamide from its different formulations.

It is well, known that dissolution is frequently the controlling step in the gastroiatestinal absorption of drugs from a solid dosage form. Since the dissolution process precedes the absorption process, any factor influencing the rate of dissolution must influence also the rate of absorption.

A number of slightly water - soluble sulph drugs in solid state dispersion in a physiologically inert-soluble carrier were prepared as a means for increasing their rate of dissolution or absorption.

Salib et al[1], studied the dissolution rate of sulphamethoxydiazine solid dispersion in polyethylene glycol[6000]

and 20,000 enhanced the dissolution rate of sulphamethoxydiazine. Sekiguck, et al[2], investigated the dissolution rate of sulphathiazole solid dispersion with urea, it was found that the dissolution rate will be diminished in the presence of urea due to its decreasing solubility in aqueous solution of urea. Simonelli et al[3], studied the enhancenent of dissolution rate of sulphathiazole by polyvinylpyrrolidone from compressed tablets of polyvinylpyrrolidone-sulphathiazole coprecipitates. Coprecipitates of sulphamethiazole and sulphisoxazole were prepared at various ratios by sekikawa et al[4].

The purpose of this work is to study the dissolution rate of sulphapyridine, sulphamerazine and sulphisoxazole from their solid dispersions using polyethylene glycol 4000 and 6000 at different ratios, as well as, their coprecipitate with polyvinylpyrrolidone.

EXPERIMENTAL

Materials:

Sulphapyridine, sulphamerazine, and sulphisoxazole and PvP 25,000 were obrained from Cid Pharmaceutical Co., Cairo , Egypt.

Gelatin capsules were obtained from, Park Davis, Co., U.S.A. All other chemicals were obtained from B,D,E, Poole U.K.

The experimental work carried out in this study comprised the following:

A- Preparation of solid dissersion.

This was prepared by the melting procedure as follows:

The polyethylene glycol 4000 and 6000 were accurately weighed, powdered , and melted in a suitable porcelain

dish. The calculated amount of the powdered drugs were then accurately weighed and added to the melted polymer with constant stirring. Cooling was effected at room temperature and the product was placed in desiccator over silica gel. The solidified product was then transferred to a suitable clean mortar, powdered and passed through sieve 8ε micron mesh size. It could be noted that the incorporation of the drugs in the melted polymar resulted in a one phase system, where by the drug disappeared in the melted polyethylene glycol, forming a solid dispersion in the polymar.

B- Preparation of coprecipitate.

This was prepared by solvent method as follows:

The polyvinylpyrrolidone(25,000) was acourately weighed and dissolved in a 100 ml absolute ethyl alcohol. The powdered drugs were accurately weighed and dissolved in another 100 ml of absolute ethyl alcohol by the aid of magnetic stirrer. The two solutions of the drug and carrier were mixed together in percelain dish, the solvent was evaporated and the residue kept in an incubator at 40 ^{o}C till constant weight. The mass was placed in desiccator over silica gel and then transferred to a suitable clean mortar, powdered and passed through sieve 80 micron mesh size.

C- Dissolution rate study.

This was carried out using an in-vitro dissolution apparatus described by USP. The calculated amount (100 mg) of powdered drug contained in gelatin capsule was rapidly introduced.Hydrochloric acid 0.1 N e was used and absorption was read at 265, 269, and 263 nm for sulphapyridine, slphisoxazole and sulphamerazine respectively, samples for analysis were obtained at suitable time(20 minutes) intervals up to aperiod of three hours, samples, each of (2 ml),were

pipetted for the spectrophotometric assay, which were replaced by an equal volume of a fresh solution of 0.1 N hydrochloric acid. No change in λ for the different drugs was observed in the presence of the various polymars.

All samples were carried out in triplicates, from which the mean values were calculated.

RESULTS AND DISCUSSION

Figure (1) shows the dissolution profiles of sulphapyridine- polyethylene glycol 4000, polyethylene glycol 6000 and polyvinylpyrrolidone coprecipitate, at 1:1 ratio of drug to polymers, physical mixture and ratio drug to polymars, physical mixture and that of sulphamerazine alone. The dissolution rate of sulphamerazine in solid dispersion physical mixture and coprecipitate was remarkably enhanced as compared with the dissolution rate from the powdered drug. Physical mixture at 1:1 ratio produced faster drug dissolution than from sulphamerazine alone or solid dispersion and coprecipitate.

On the other hand, sulphamerazine solid dispersion in polyethylene glycol 4000 in both ratios (1:1 and 1:3), have dissolution rate higher than the dissolution rate of the drug dispersed in polyethylene glycol 6000 at different ratio as shown in Figure 3 and 4. This finding could be attributed to the viscosity of the dissolution medium. The relative lower viscosity of the polyethylene glycol 4000 solution could be considered an important factor, as mentioned before.

The dissolution study on the physical mixtures containing both ratios (1:1 and 1:3) as illustrated in Figures 3 and 4, shows enhancement in the dissolution rate of the

sulphamerazine from the physical mixture, as compared with that of the powdered drug. It was suggested that the main contributing factor influencing the enhancement in the dissolution rate of the drug incorporated in physical mixtures could be the presence of overlapping diffusion layers of the drug and soluble carrier.

Figures (5) and (6), shows the dissolution profiles of sulphisoxazole polyethylene glycol 4000, 6000 and polyvinylpyrrolidone (25,000) coprecipitate at (1 : 1) and (1 : 3) ratios drug to polymars, physical mixture and that of sulphisoxazole alone. The results obtained follow the same pattern as for the two previousely mentioned sulphapyridine and sulphamerazine. In this case, it was expected that the same interpretations could be valid for the results of dissolution obtained on investigating other preparations containing sulphisoxazole. The difference in the rate of dissolution between the various formulations of the drugs investigated may be due to the difference in their water solubility. Other factors such as variations in the molecular structure between the different drugs may also play a part.

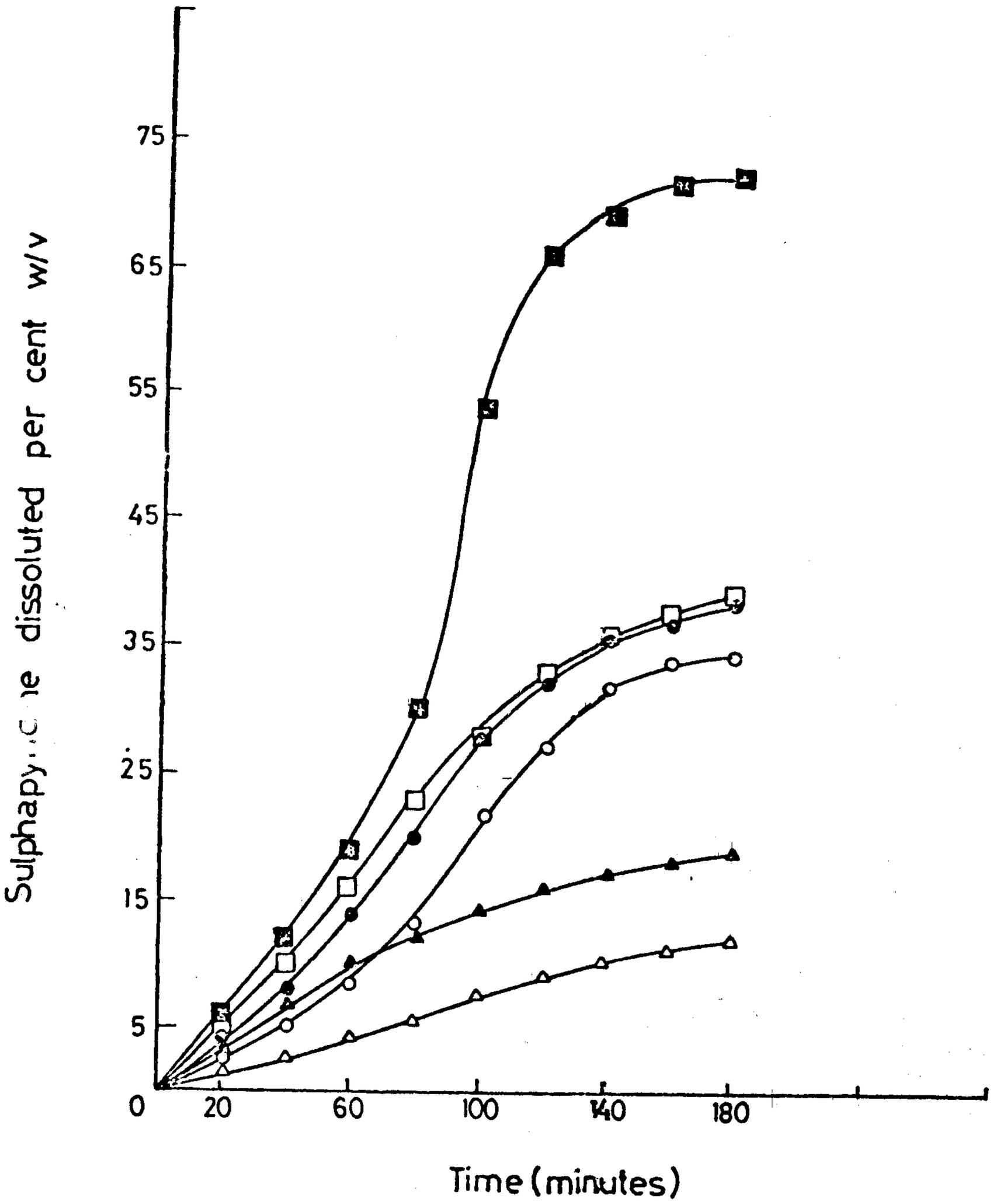

Fig.1. Dissolution rate of sulphapyridine from its (1:1) physical mixtures; solid dispersions and coprecipitates.

Key: △ Pure drug. ▲ Coprecipitate-PVP. o Solid dispersion-PEG 6000

● Physical mixture-PEG 6000. □ Solid dispersion-PEG 4000.

■ Physical mixture-PEG 4000.

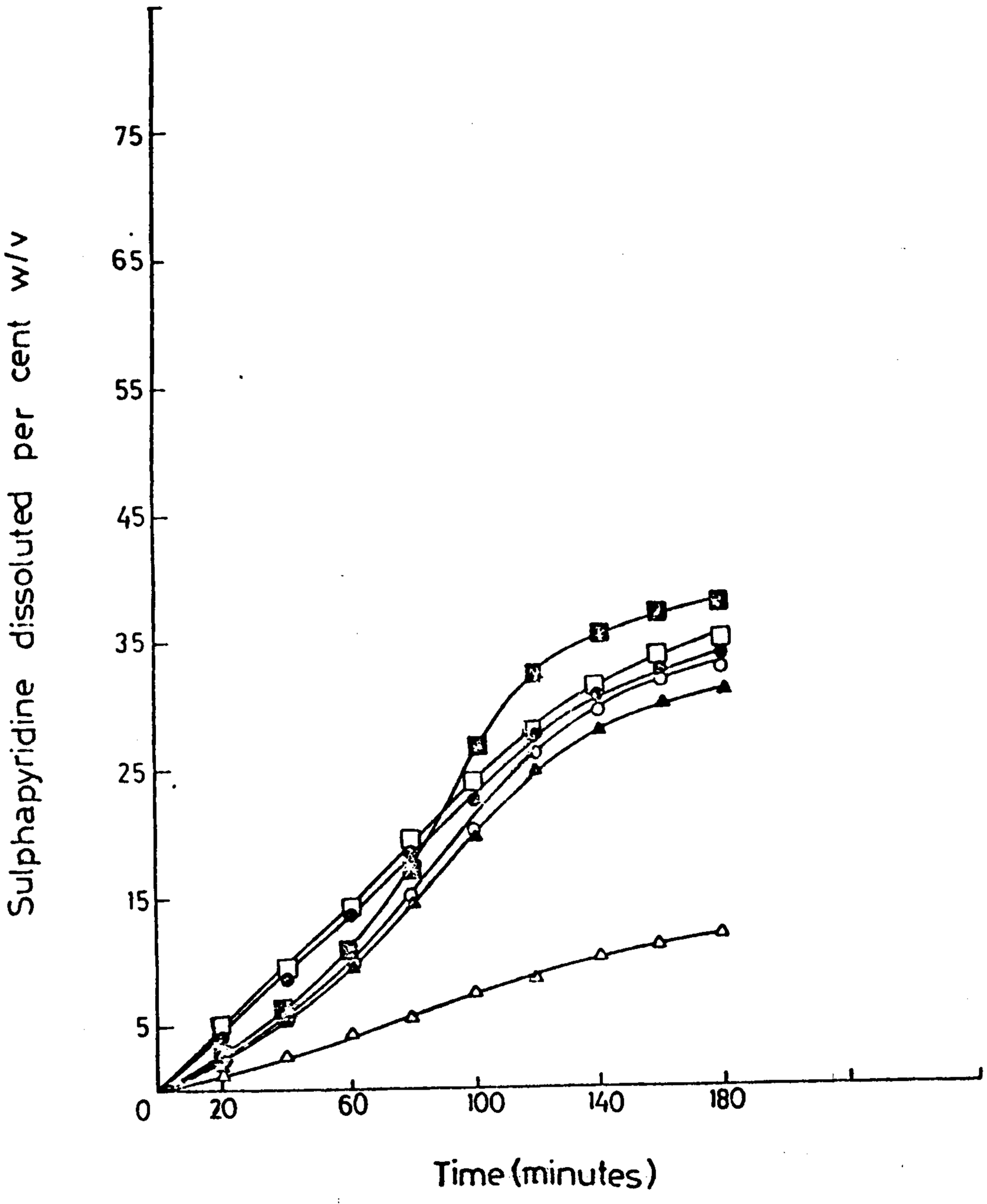

Fig.2. Dissolution rate of sulphapyridine from its (1:3) physical mixtures; solid dispersions and coprecipitates.

Key: △ Pure drug. ▲ Coprecipitate-PVP. o Solid dispersion-PEG 6000.

● Physical mixture-PEG 6000. □ Solid dispersion-PEG 4000.

■ Physical mixture-PEG 4000.

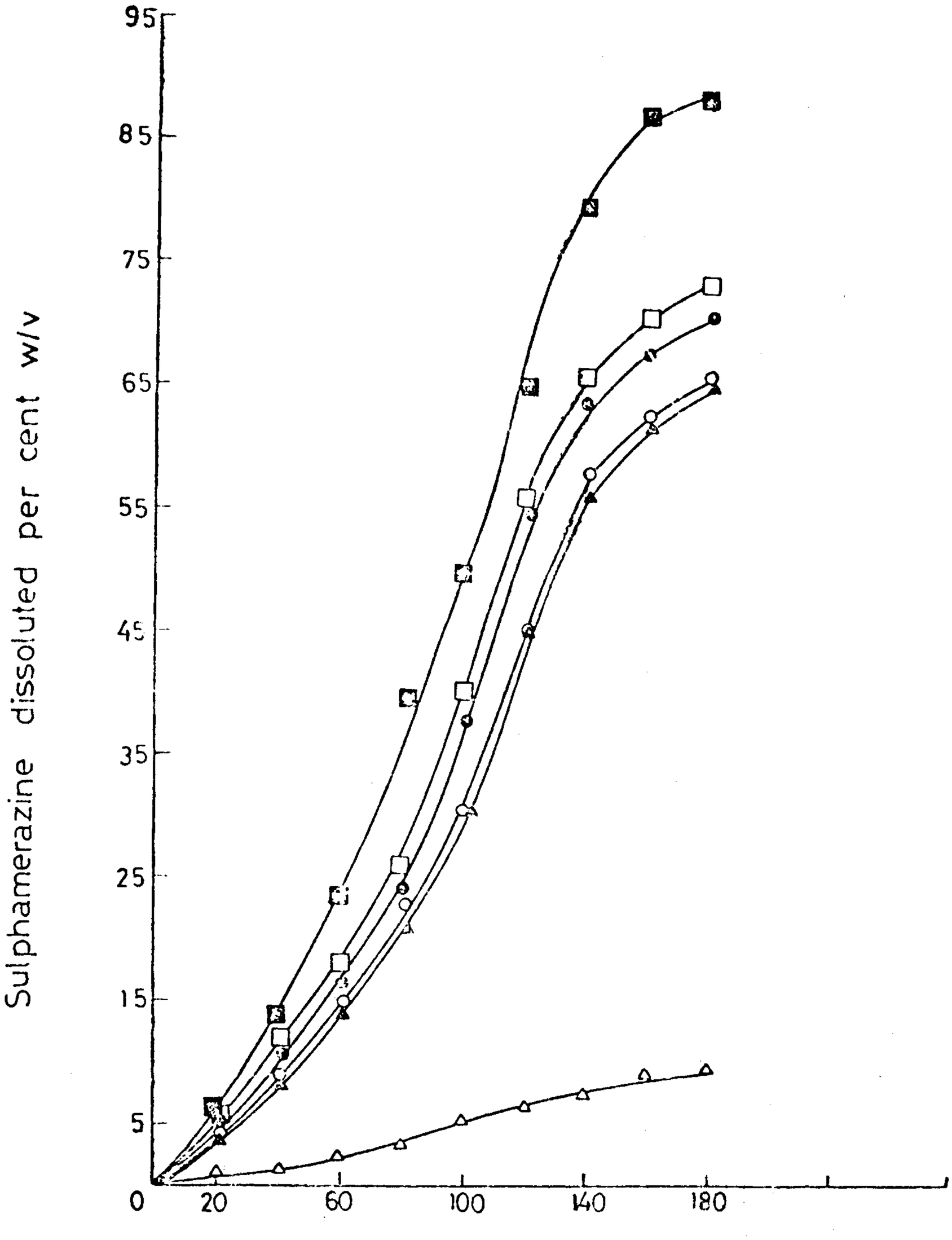

Fig.3. Dissolution rate of sulphamerazine from its (1:1) physical mixtures; solid dispersions and coprecipitates.

Key: Δ Pure drug ▲ Coprecipitate-PVP o Solid dispersion-PEG 6000.
● Physical mixture-PEG 6000 □ Solid dispersion-PEG 4000.
■ Physical mixture-PEG 4000.

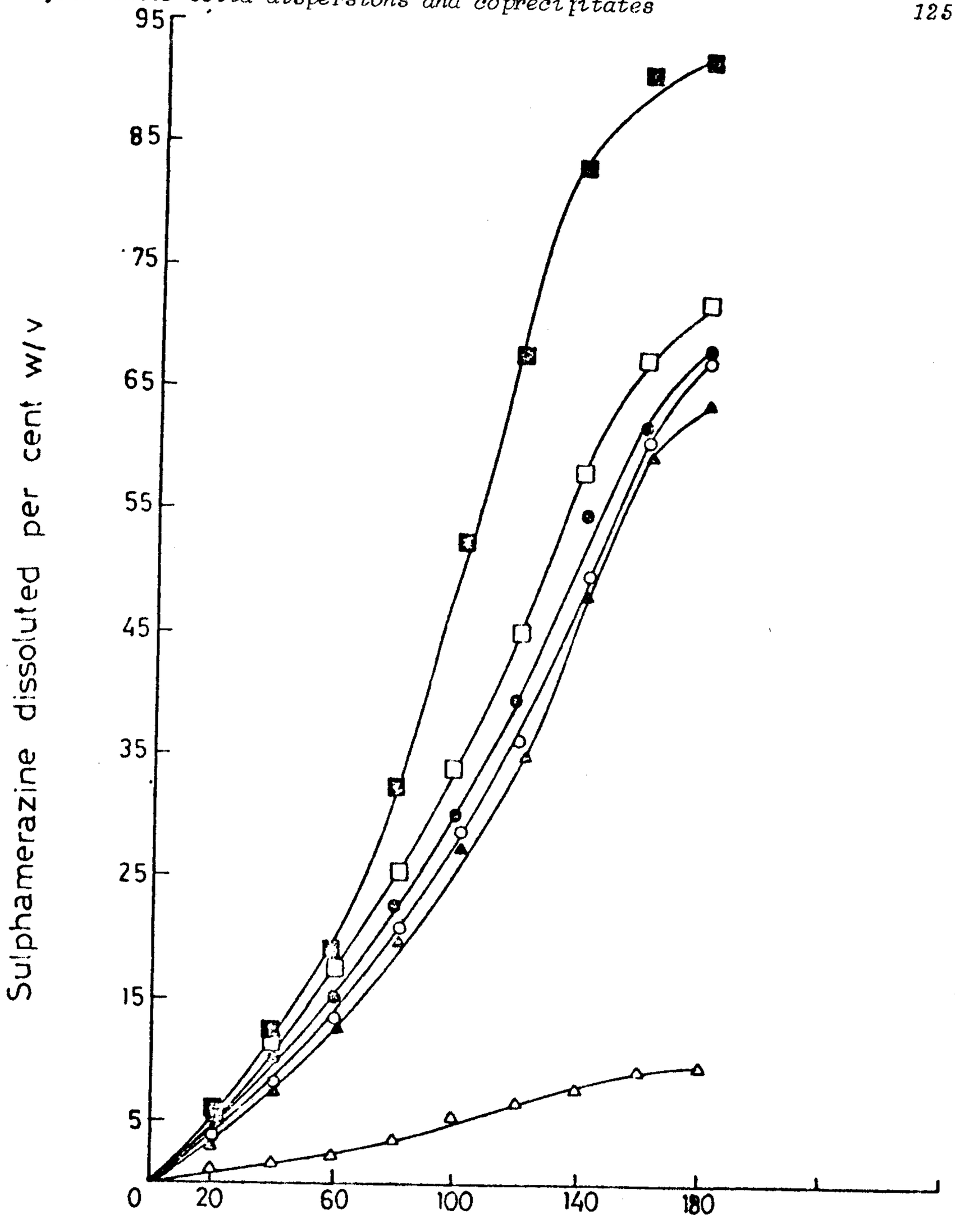

Fig.4. Dissolution rate of sulphamerazine from its (1 : 3) physical mixtures; solid dispersions and coprecipitates.

Key: △ Pure drug. ▲ Coprecipitate-PVP. ○ Solid dispersion- PEG 6000.
● Physical mixture- PEG 6000. □ Solid dispersion- PEG 4000.
■ Physical mixture- PEG 4000.

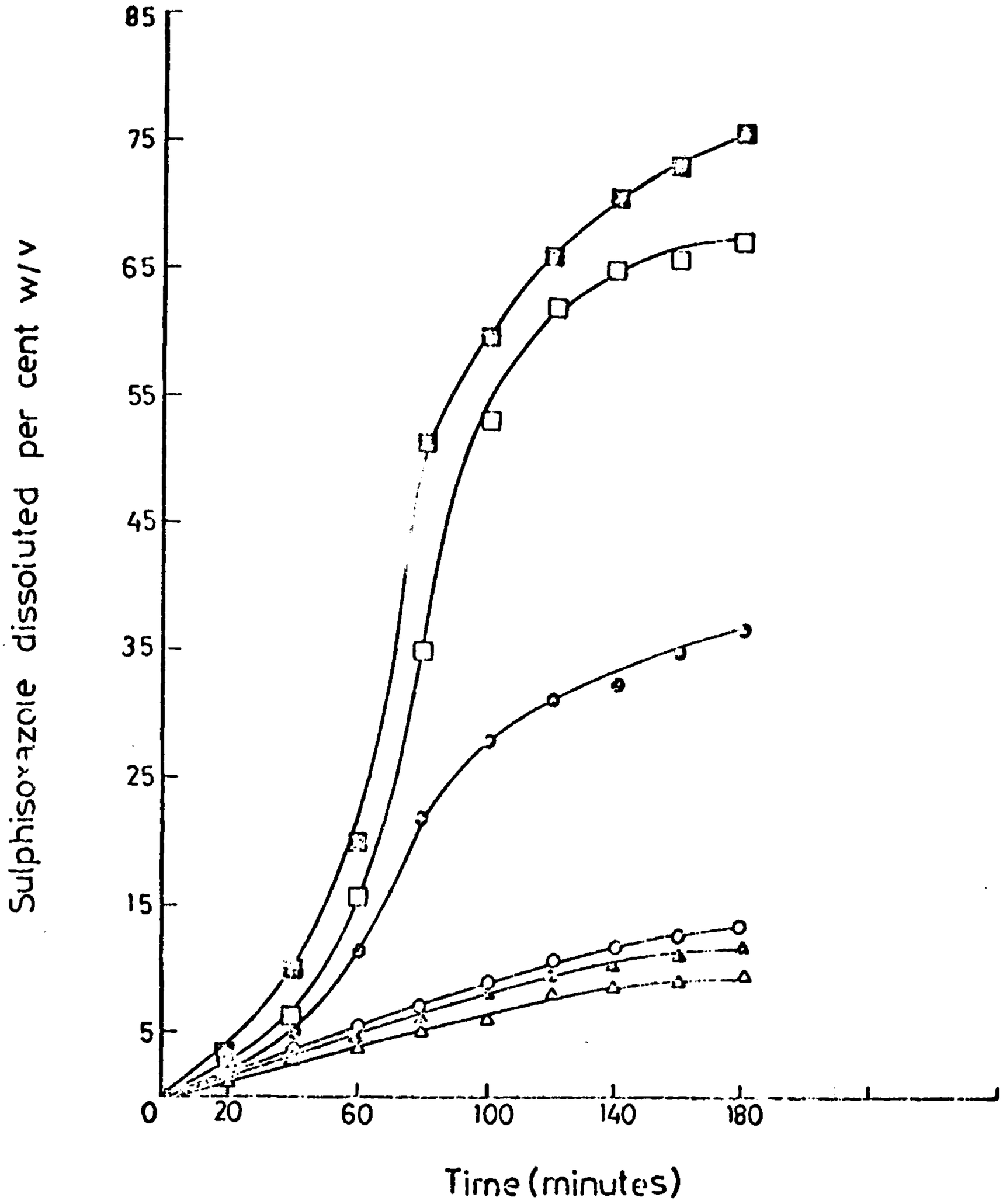

Fig.5. Dissolution rate of sulphisoxazole from its (1:1) physical mixtures; solid dispersions and coprecipitates.

Key: △ Pure drug. ▲ Coprecipitate-PVP. o Solid dispersion-PEG 6000.
● Physical mixture-PEG 6000. □ Solid dispersion-PEG 4000.
◘ Physical mixture-PEG 4000.

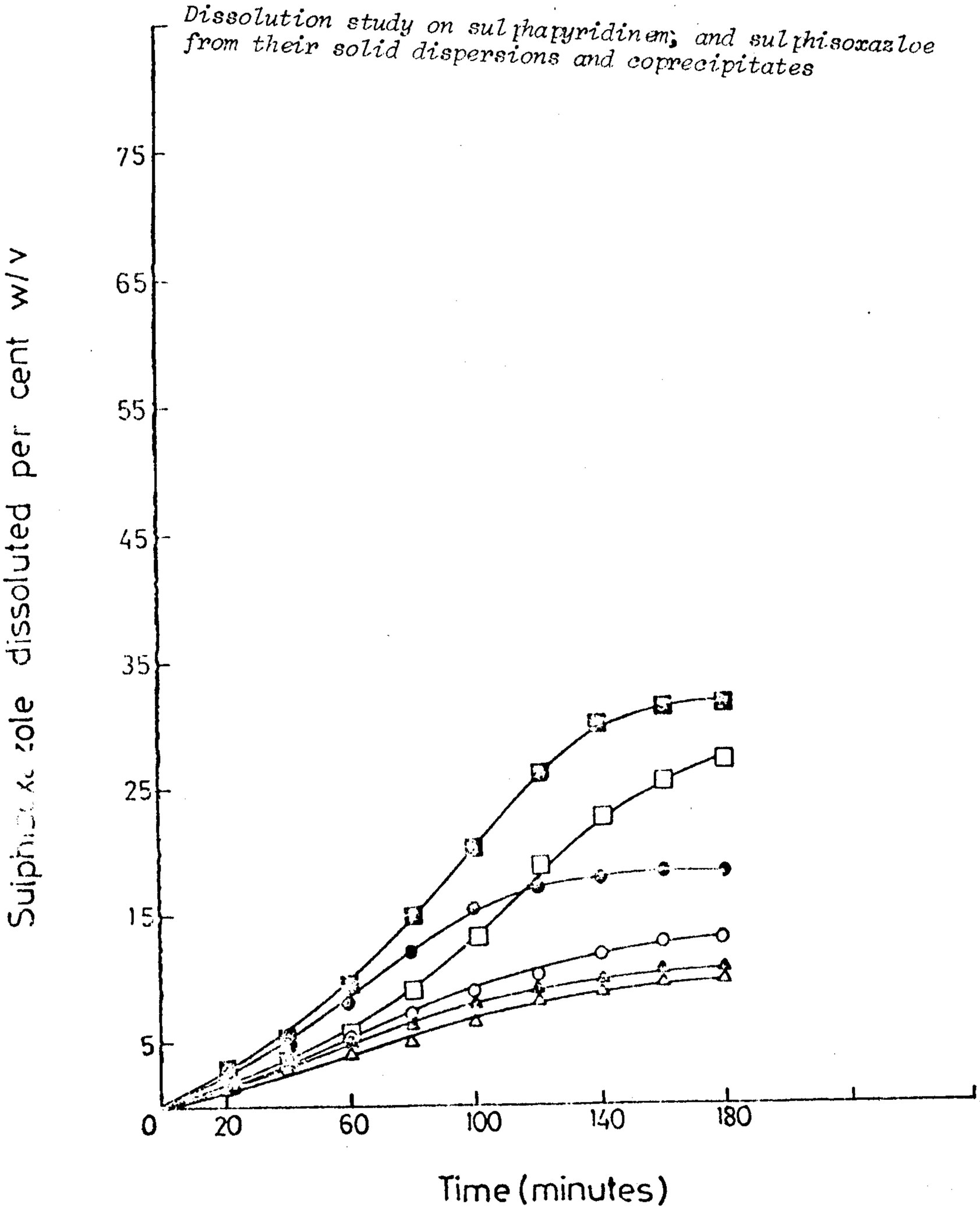

Fig.6. Dissolution rate of sulphisoxazole from its (1:3) physical mixtures; solid dispersions and coprecipitates.

Key: △ Pure drug. ▲ Coprecipitate-PVP. ○ Solid dispersion-PEG 6000.
● Physical mixture-PEG 6000. □ Solid dispersion-PEG 4000.
■ Physical mixture-PEG 4000.

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دراسة على اتاحة السلفا بيريدين والسلفاميرازين والسلفاسكسازول من المشتتات الصلبة والمترسبات المختلفـــة

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معدل الاتاحة للسلفابيريدين والسلفاميرازين والسلفاسكسازول درست من المشتتات الصلبة باستعمال عديد الايثيلين جليكول ٤٠٠٠ ، وعديد الايثيلين جليكول ٦٠٠٠ والمترسبـات باستعمال عديد الفينيل بيروليدون ٢٥٠٠٠ . ولقد وجد ان معدل الاتاحة اكثر بكثيـر من المستحضرات التى تحتوى على مشتتات صلبة او مترسبات للثلاث سلفات المختلفة .

وقد وجد ان نسبة البوليمر الى العقار وكذلك التركيب الجزئى للبوليمرات وكذلك طبيعتـه تؤثـر على معدل الاتاحـة بنسبة مختلفة لكل سلفا وذلك من مختلف التراكيب التى تـتم تحضيـرها .

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