# DISPERSIONI

**Fase continua acquosa (P.A. nella fase dispersa)**
**Diluizione nei liquidi digestivi**

## EMULSIONI

finezza

viscosita' fase oleosa

coeff. di ripart. olio/liquidi digestivi

possibili interazioni con agenti di viscosita'

ruolo del tensioattivo (solubilizz. micellare-complessi)

diffusione del p.a. dalla fase dispersa verso la fase continua digestiva

## SOSPENSIONI

forme cristalline

viscosita':
- strutturale
- dovuta ad agenti viscosanti

*az. del tensioattivo (bagnabilità)

dissoluzione del p.a. a partire da particelle

p.a. in soluz. in fase continua: rischio di assorbim.

## PRINCIPIO ATTIVO SOLUBILIZZATO nei liquidi digestivi

caratteristiche di asserbibilita' proprie del p.a.

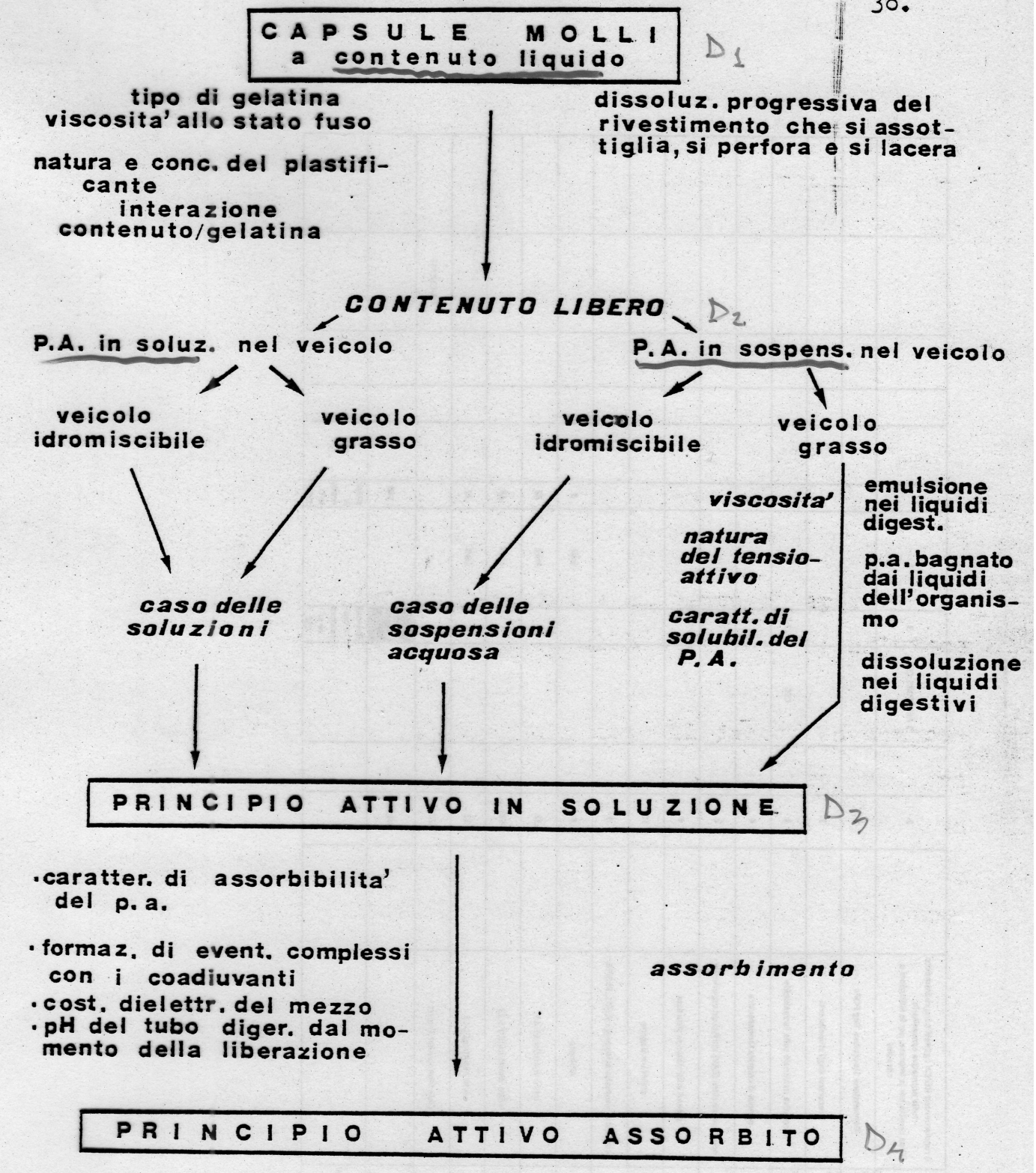
modif. dovute al tensioattivo

*della membrane*

*assorbimento*

## PRINCIPIO ATTIVO ASSORBITO

*Fattori che influenzano la messa a disposizione di un p.a. a partire da dispersioni*




Massa a disposizione del p.a. a partire dalle caps. molli e fattori che la influenzano

Fig. 6.

**CAPSULE DI GELATINA** $D_1$

tipo di gelatina
interazione contenuto/gelatina
invecchiamento

↓

rottura dell'involucro ai due poli

Cilindro di gelatina che riveste la polvere

porosita'
- ·dimens. particelle
- ·tipo di macchina

bagnabilita'
- ·caratterist. di idrofilia della polvere
- ·coadiuvanti
  - idrofilia
  - pot. assorbente
  - pres. tensioattivo
- ·condiz. di «mescolazione»

↓

penetrazione progressiva del liquido nella polvere

dissoluz. dell'involucro di gelatina

Magma di polvere piu' o meno bagnata $D_2$

↓

disaggregazione della massa di polvere dopo che e' stata bagnata dai liquidi digestivi

dissoluz. del p.a. bagnato

**PRINCIPIO ATTIVO IN SOLUZIONE** $D_3$

caratterist. di assorbibilita' proprie del p.a.
liberaz. e dissoluz. del p.a. prima della zona di assorbimento ottimale

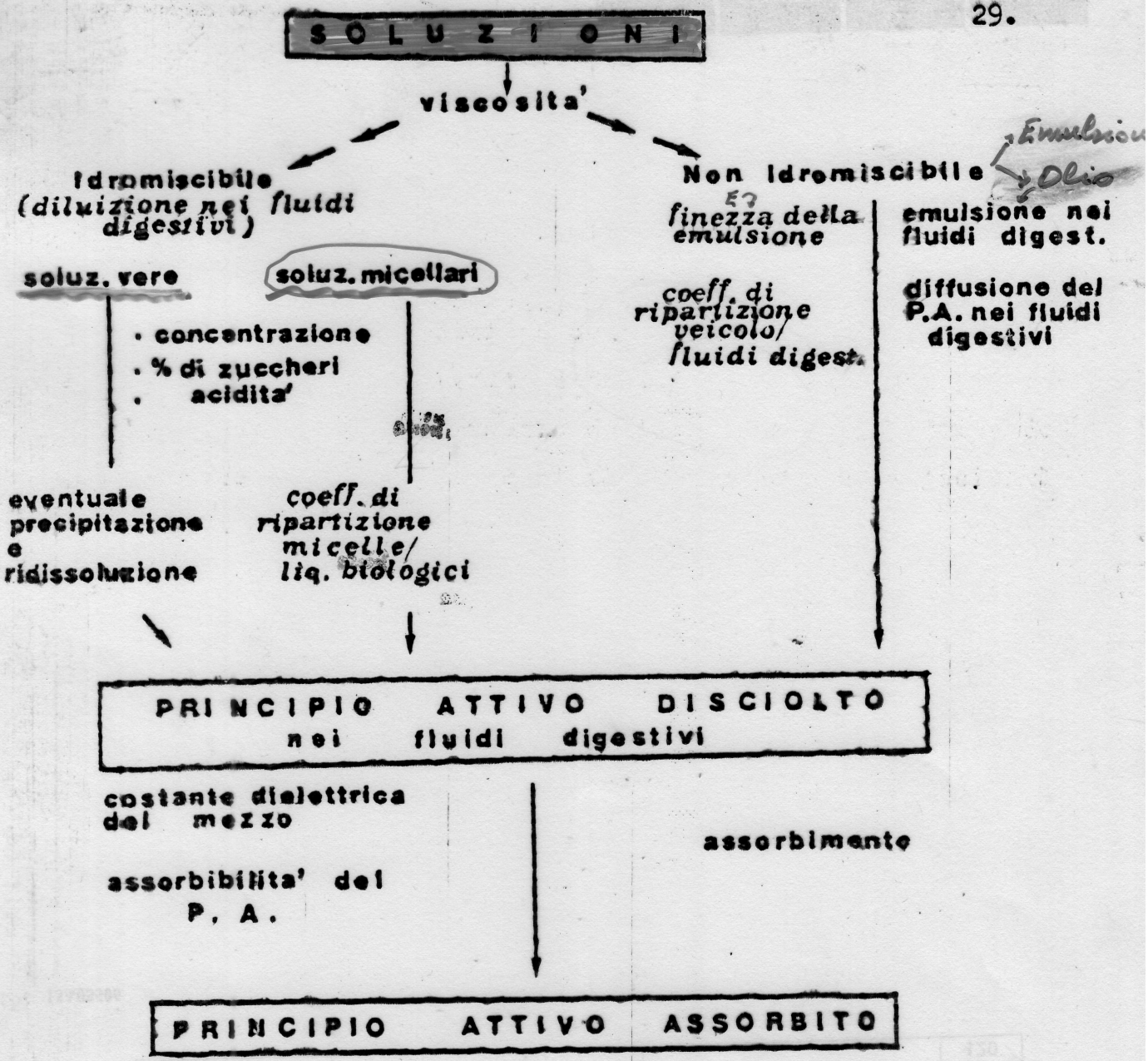
↓

assorbimento

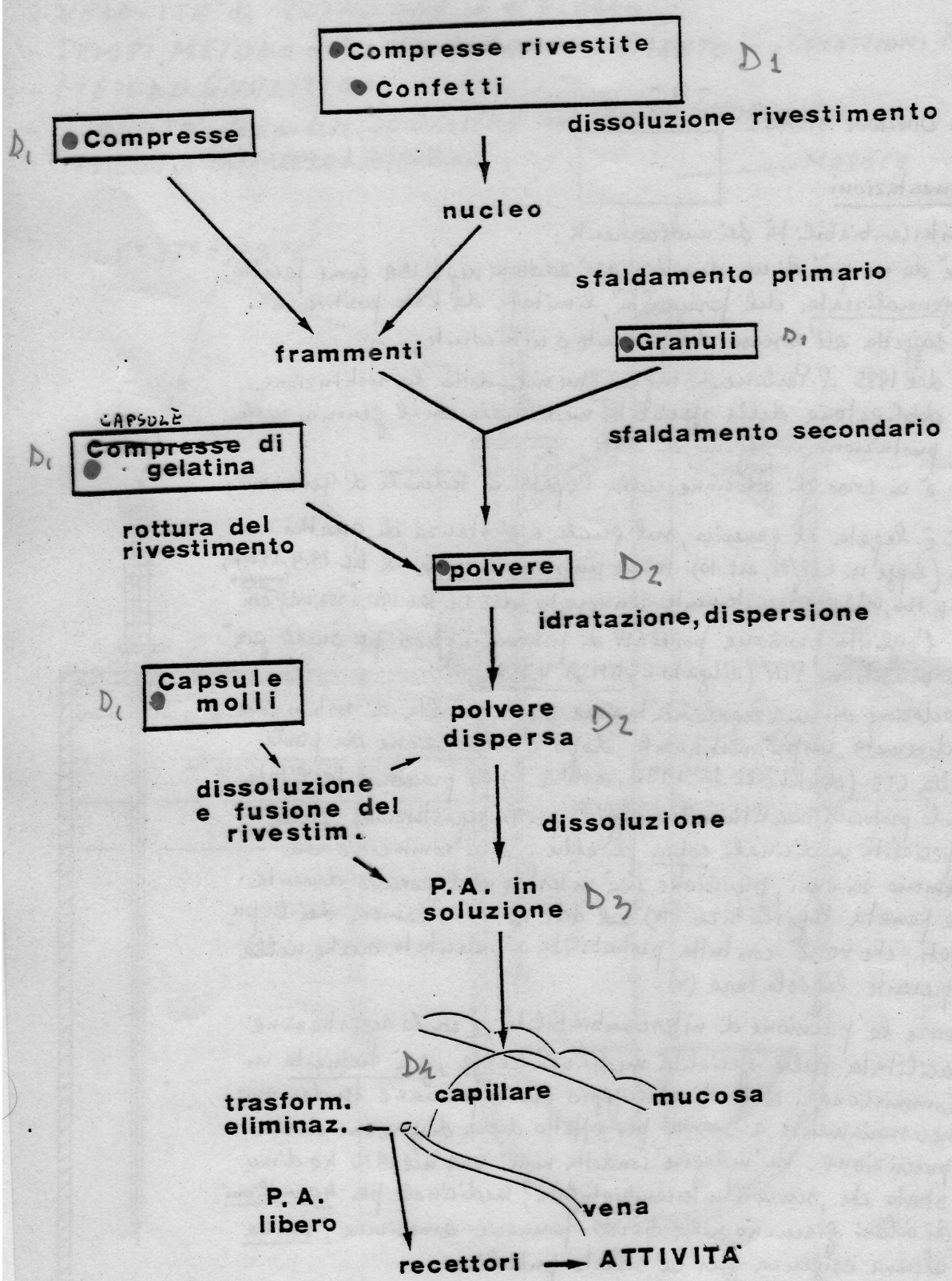
**PRINCIPIO ATTIVO ASSORBITO** $D_4$

Messa a disposizione del p.a. a partire dalle caps. di gelatina e fattori che la influenzano

Fig. 7.




**Messa a disposizione dell' organismo del P.A. a partire da soluzioni e fattori influenzanti.**




Messa a disposizione dell'organismo del P.A. a partire da forme orali

Fig. 3.

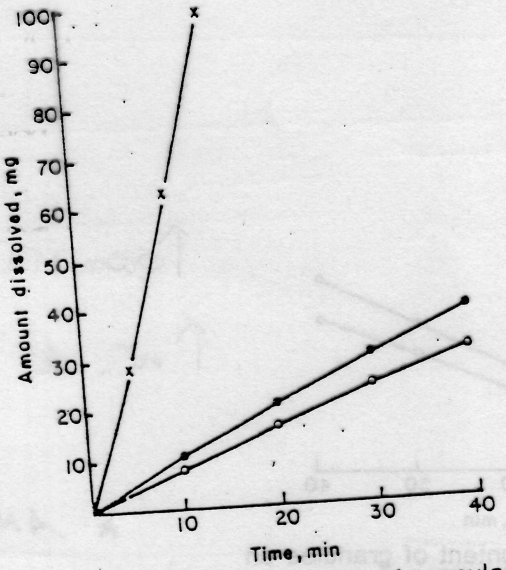



**Fig 5-1.** Effect of starch content of granules on dissolution rate of salicylic acid contained in compressed tablets. [Reproduced from Levy, *et al*, *J Pharm Sci*, *52*, *1050* **(1963).**]

*Key:* O, 5%; ●, 10%; X, 20% starch in granules.

**Table 5-1—Diazepam Tablet Formulations with Variable Swelling Capacities of Diluents**

| Ingredient, % (w/w) | Formulation | | | |
|---|---|---|---|---|
| | P-2 | P-30 | S-2 | S-30 |
| Diazepam | 2.5 | 2.5 | 2.5 | 2.5 |
| Dicalcium phosphate dihydrate | 77 | 77 | 93 | 93 |
| Potato starch | 20 | 20 | | |
| Sodium starch glycolate | | | 4 | 4 |
| Magnesium stearate | 0.5 | 0.5 | 0.5 | 0.5 |
| Mixing time with magnesium stearate (min) | 2 | 30 | 2 | 30 |

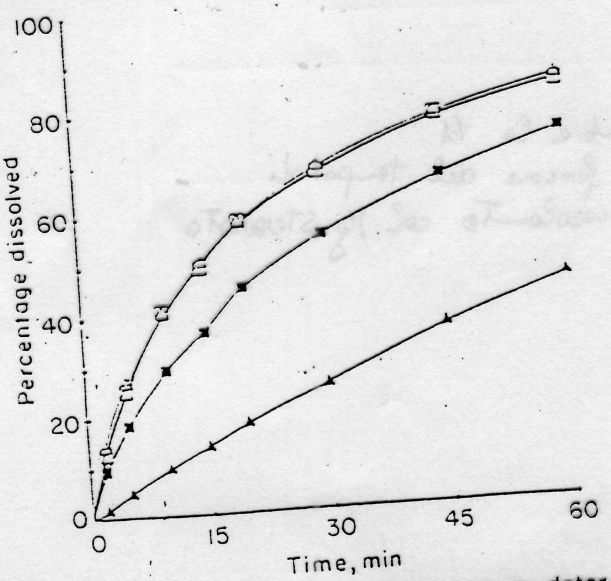



**Fig 5-2.** Dissolution profiles of diazepam, determined with the rotating basket at 100 rpm. [Reproduced from Proost, *et al*, *Int J Pharm*, *13*, 287 **(1983).**]

S-30 (abbreviations see Table

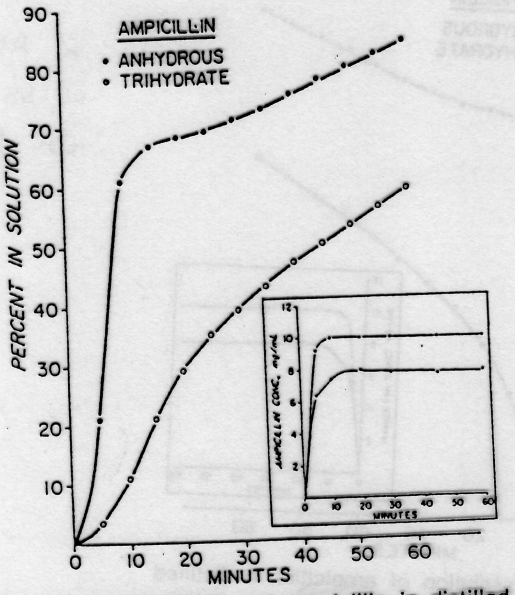



**Fig 4-10a.** Dissolution of ampicillin in distilled water at 37°C from trade capsule formulations. *Inset:* Solubility of ampicillin, anhydrous and ampicillin trihydrate in distilled water at 37°C. [Reproduced from Poole, *Curr Ther Res*, *10*, 292 (1968).]

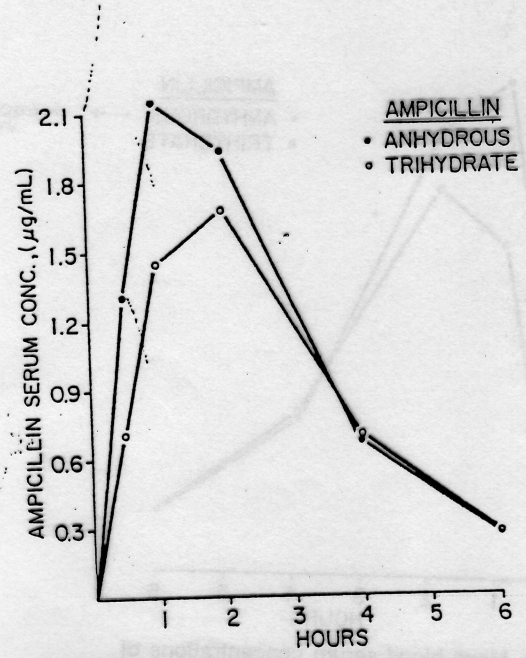



**Fig 4-10b.** Mean blood serum concentrations of ampicillin in human subjects after oral administration of 250 mg doses of the oral suspensions. [Reproduced from Poole, *Curr Ther Res*, *10*, 292 (1968).]

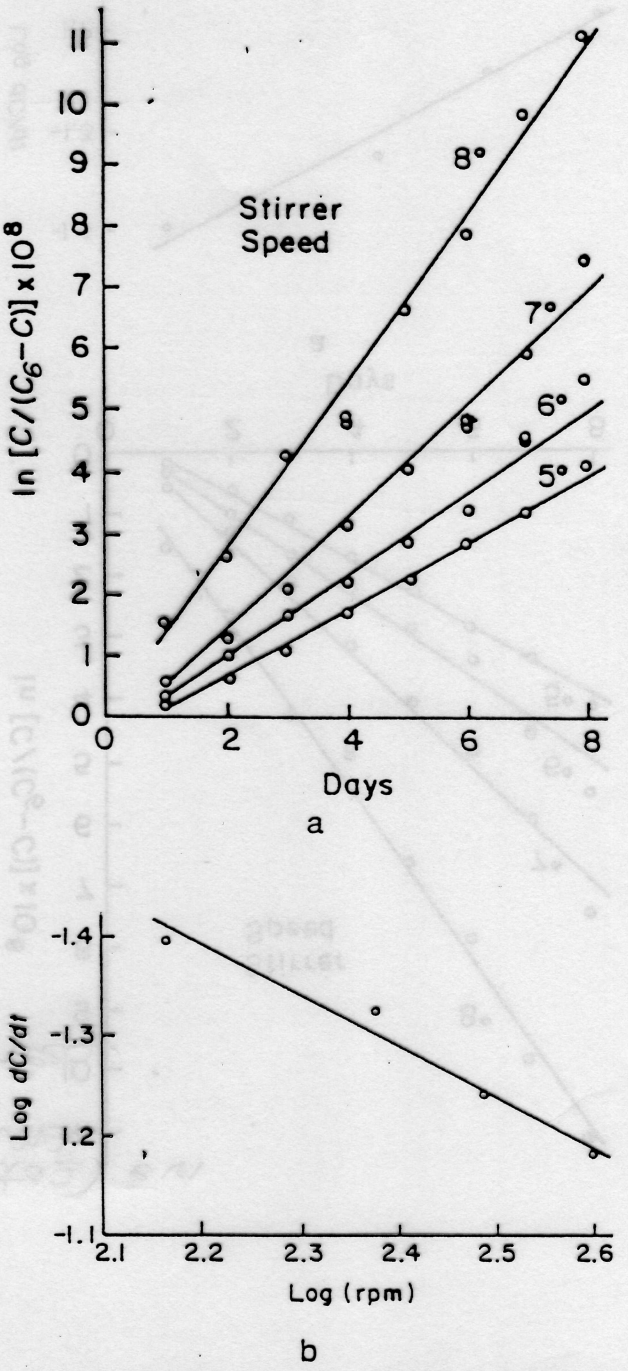



**Fig 2-15. a:** Triamcinolone acetonide dissolution in distilled water, plotted in accordance with the integrated form of the modified Noyes-Whitney equation. 5 = 147 rpm; 6 = 248 rpm; 7 = 308 rpm; 8 = 398 rpm. **b:** Log-log plot of triamcinolone acetonide dissolution rate in distilled water vs stirrer speed (rpm). [Reproduced from Block and Patel, *J Pharm Sci*, *62*, 617 (1973).]

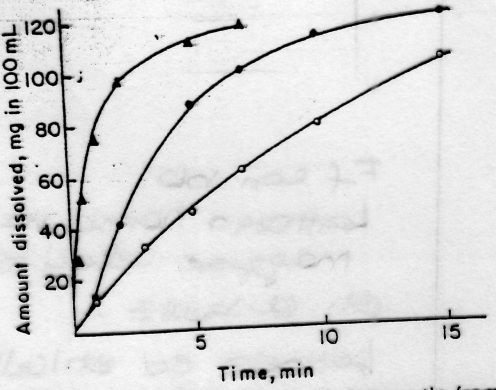



**Fig 5-3a.** Rate of dissolution of phenacetin from powder, granules, and tablets in diluted gastric juice (surface tension 42.7 dynes $cm^{-1}$, pH 1.85). [Reproduced from Solvang and Finholt, *J Pharm Sci*, *59*, 50 (1970).]

*Key:* O, phenacetin powder; ▲, phenacetin granules; ●, phenacetin tablets.

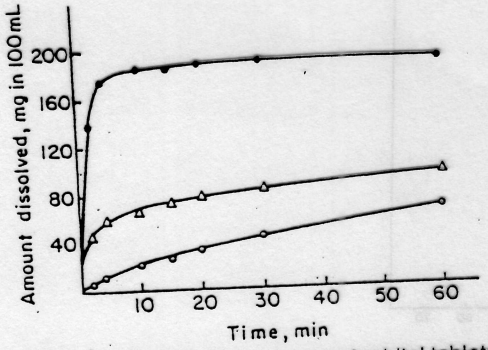
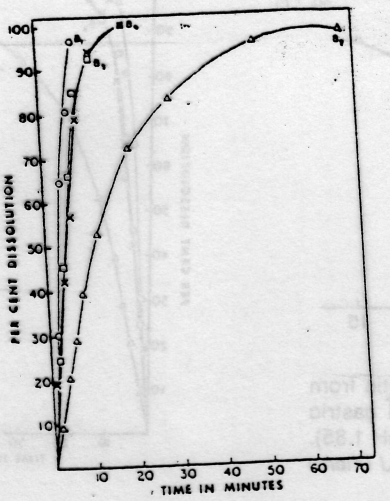
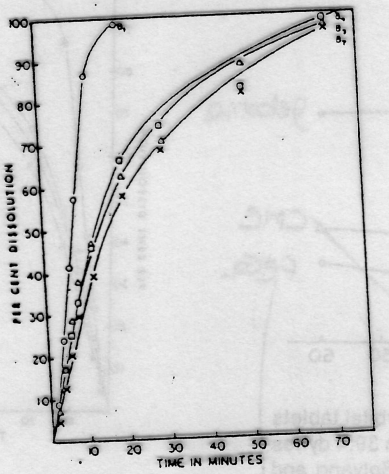



**Fig 5-3b.** Dissolution rate of phenobarbital tablets in diluted gastric juice (surface tension 39.4 dynes $cm^{-1}$, pH 1.50). [Reproduced from Solvang and Finholt, *J Pharm Sci*, *59*, 50 (1970).]

*Key:* ●, gelatin binder; △, CMC; O, polyethylene glycol 6000.




a




b

**Fig 5-4. a:** Comparison of filler-binders in a tablet formula containing starch, hydrogenated vegetable oil, and 3.5 S-C hardness. **b:** Comparison of filler-binders in a tablet formula containing no starch, magnesium stearate, and 6.5 S-C hardness. [Reproduced from Marlowe and Shangraw, *J Pharm Sci*, *56*, 500 (1967).]

*Key:* $B_1$, spray-dried lactose; $B_2$, ethylcellulose and lactose; $B_3$, acacia mucilage and lactose; $B_4$, starch paste and lactose.

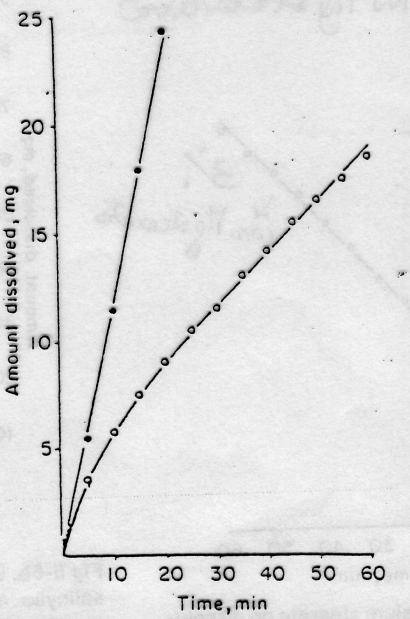



**Fig 5-5a.** Effect of magnesium stearate on dissolution rate of salicylic acid from rotating disks made from fine salicylic acid powder. [Reproduced from Levy and Gumtow, *J Pharm Sci*, *52*, 1140 (1963).]

*Key:* O, 3% magnesium stearate; ●, no lubricant added.

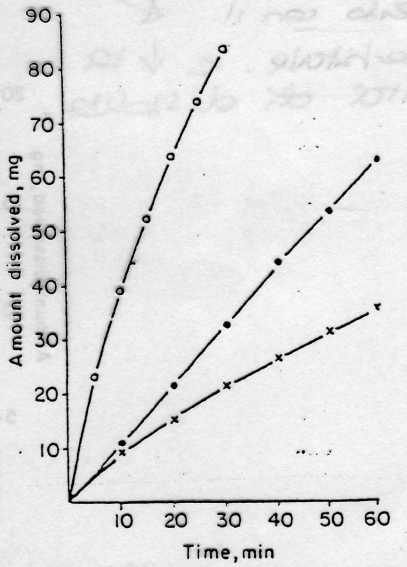



**Fig 5-5b.** Effect of lubricant on dissolution rate of salicylic acid contained in compressed tablets (formula A). [Reproduced from Levy and Gumtow, *J Pharm Sci*, *52*, 1140 (1963).]

*Key:* X, 3% magnesium stearate; ●, no lubricant; O, 3% sodium lauryl sulfate.

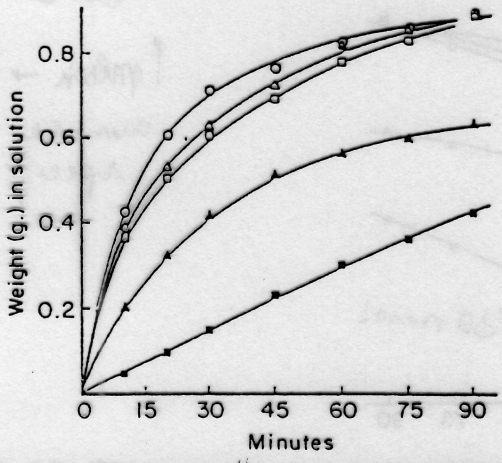



**Fig 4-7a.** Effect of particle size on dissolution of salicylic acid under sink conditions using four propellers at 30 rpm and 37°C. [Reproduced from Ismat Ullah and Cadwallader, *J Pharm Sci*, *59*, 979 **(1970).**]

*Key:* O; 200/230 mesh; Δ, 120/140 mesh; □ 60/80 mesh; ▲, 40/60 mesh; ■, 20/30 mesh.

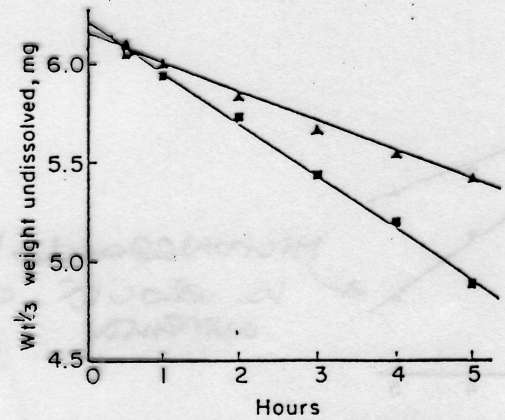



**Fig 4-7b.** Plots of $Wt^{1/3}$ vs time. [Reproduced from Ismat Ullah and Cadwallader, *J Pharm Sci*, *60*, 230 230 **(1971).**]

*Key:* ▲, regular milled griseofulvin powder; ■, micronized griseofulvin powder.

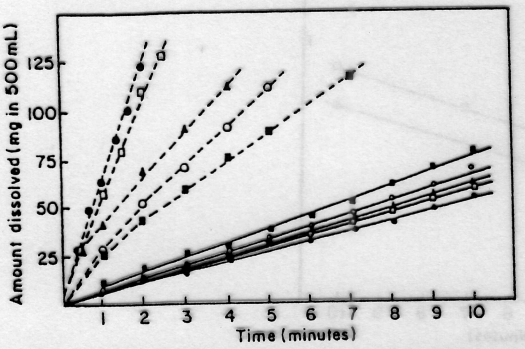



**Fig 4-9a.** Effect of particle size on rate of dissolution of phenacetin. [Reproduced from Finholt, *et al*, *Medd Norsk Farm Selsk*, *28*, 17 **(1966).**]

*Key:* ● particle size, 0.11–0.15 mm; □ particle size, 0.15–0.21 mm; ▲ particle size, 0.21–0.30 mm; O particle size, 0.30–0.50 mm; ■ particle size, 0.50–0.71 mm; — dissolution medium; 0.1*N* HCl; – – – dissolution medium, 0.1*N* HCl containing 0.2% Tween 80.

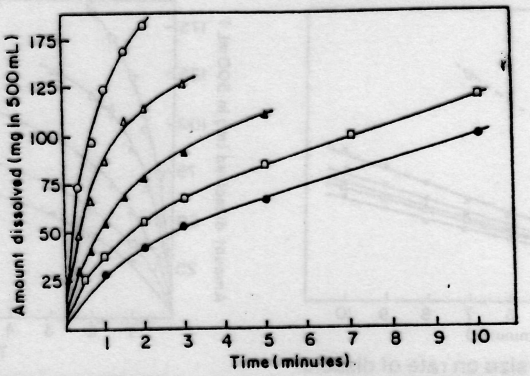



**Fig 4-9b.** Effect of particle size of phenacetin on dissolution rate of the drug from granules. [Reproduced from Finholt, *et al*, *Medd Norsk Farm Selsk*, *28*, 17 **(1966).**]

*Key:* O particle size, 0.11–0.15 mm; △ particle size, 0.15–0.21 mm; ▲ particle size, 0.21–0.30 mm; □ particle size, 0.30–0.50 mm; ● particle size, 0.50–0.71 mm.

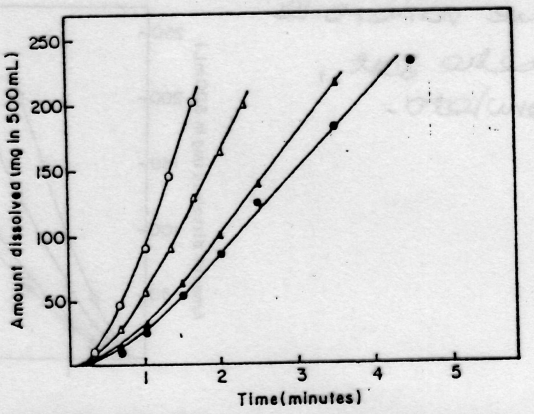



**Fig 4-9c.** Effect of particle size of phenobarbital on dissolution rate of the drug from tablets. [Reproduced from Finholt, *et al*, *Medd Norsk Farm Selsk*, *28*, 17 **(1966).**]

*Key:* O particle size, 0.07–0.15 mm; △ particle size, 0.15–0.25 mm; ▲ particle size, 0.25–0.42 mm; ● particle size, 0.42–0.71 mm.

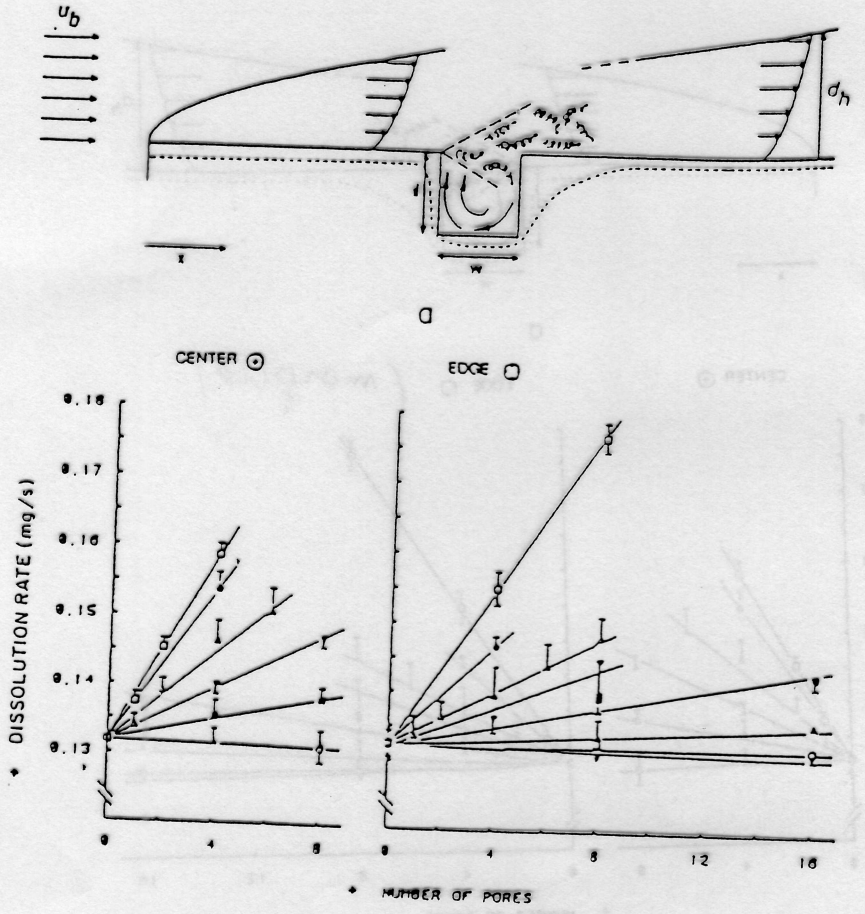



**Fig 2-5. a:** Disturbance of the hydrodynamic laminar boundary layer present along a semi-infinite plate in the vicinity of a depression. **b:** Dissolution rate of a borax tablet surface with drilled pores at 100 rpm. Vertical bars represent the standard deviation of the mean dissolution rate. [Reproduced from Grijseels and deBlaey, *Int J Pharm*, *9*, 337 (1981).]

Distance from pores to surface edge: (left) 5.0 mm (central position); (right) 2.5 mm (edge position). □, pore diameter 2.00 mm, ●, 1.50 mm; △, 1.00 mm; ▽, 0.70 mm; ■, 0.50 mm; ▲, 0.40 mm; ○, 0.30 mm; ▼, 0.20 mm.

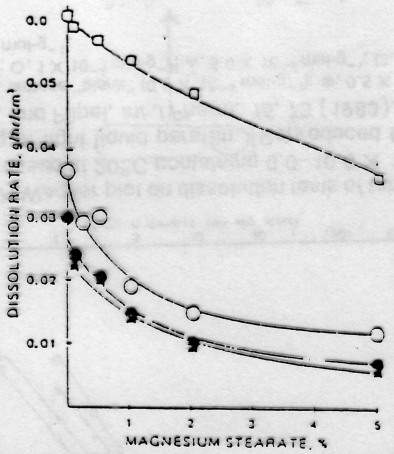



**Fig 5-6a.** Effect of concentration of magnesium stearate on dissolution rate of 80/100-mesh materials compressed at 1135 kg. [Reproduced from Iranloye, and Parrott, *J Pharm Sci*, *67*, 535 (1978).]

*Key:* O, salicylic acid; □, aspirin; ●, salicylic acid from equimolar mixture of aspirin and salicylic acid; ■, aspirin from equimolar mixture of aspirin and salicylic acid.

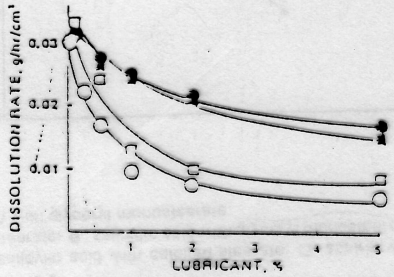



**Fig 5-6b.** Effect of concentration of calcium stearate and glyceryl monostearate on dissolution rate of 80/100-mesh equimolar mixture of aspirin and salicylic acid compressed at 1135 kg. [Reproduced from Iranloye, and Parrott, *J Pharm Sci*, *67*, 535 (1978).]

*Key:* O, salicylic acid with calcium stearate; □, aspirin with calcium stearate; ●, salicylic acid with glyceryl monostearate; ■, aspirin with glyceryl monostearate.

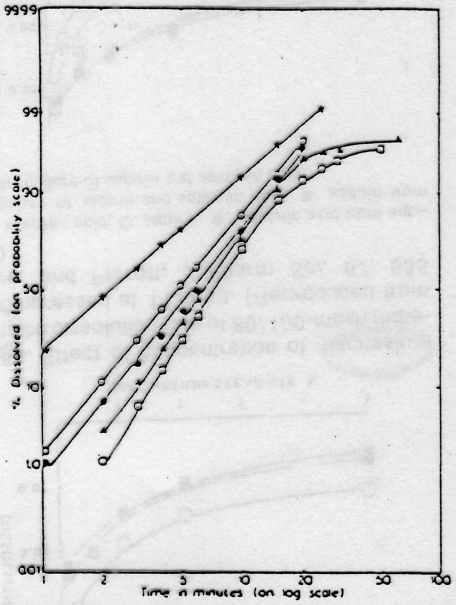



**Fig 5-7.** Wagner plot on dissolution tests of tablets compressed at 20°C containing 0.0–10.0 × $10^{-5}$ mol · g of light liquid paraffin. [Reproduced from Igwilo, and Pilpel, *Int J Pharm*, *15*, 73 (1983).]

*Key:* ★, lactose "blank" (0.0 × $10^{-5}$ mol·$g^{-1}$); ●, 0.5 × $10^{-5}$ mol·$g^{-1}$; O, 1 × $10^{-5}$ mol·$g^{-1}$; ▲, 5.0 × $10^{-5}$ mol·$g^{-1}$; □, 10.0 × $10^{-5}$ mol·$g^{-1}$.

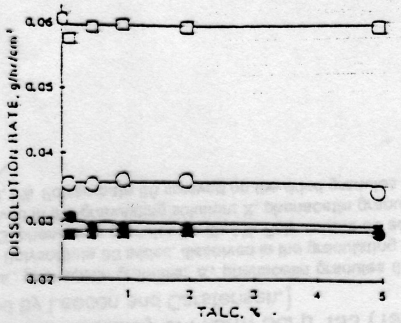



**Fig 5-6c.** Effect of concentration of talc on dissolution rate of 80/100-mesh materials compressed at 1135 kg. [Reproduced from Iranloye, and Parrott, *J Pharm Sci*, *67*, 535 (1978).]

*Key:* O, salicylic acid; □, aspirin; ●, salicylic acid from equimolar mixture of aspirin and salicylic acid; ■, aspirin from equimolar mixture of aspirin and salicylic acid.

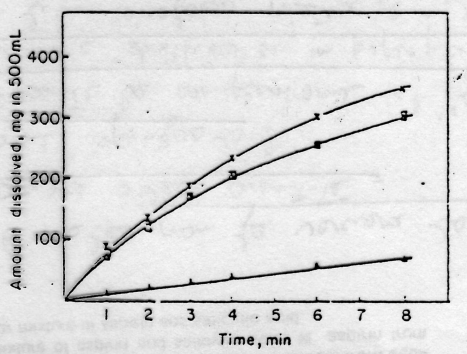



**Fig 5-8.** Effect of Polysorbate 80 on the dissolution rate of phenacetin from granules. [Reproduced from Finholt, "Dissolution Technology," published by the industrial Pharmaceutical Technology Section of the Academy of Pharm Sci p 133 (1974), edited by Leeson and Carstensen.]

*Key:* ▲, phenacetin granules; △, phenacetin granules II with 0.1% Polysorbate 80 added, dissolved in the granulating solution; □, phenacetin granules II with 1% Polysorbate 80 added, dissolved in the granulating solution; X, phenacetin granules II with 0.1% Polysorbate 80 sprayed on the dried granules.

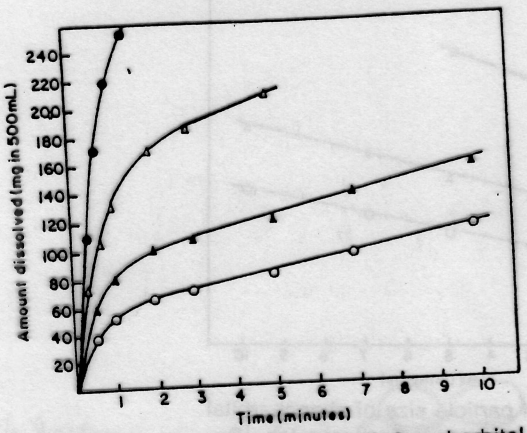



**Fig 4-8a.** Effect of particle size of phenobarbital on dissolution rate of the drug from granules. [Reproduced from Finholt, *et al*, *Medd Norsk Farm Selsk*, *28*, 17 **(1966).**]

*Key:* ⊖ particle size, 0.07–0.15 mm; △ particle size, 0.15–0.25 m; ▲ particle size, 0.25–0.42 mm; ○ particle size, 0.42–0.71 mm.

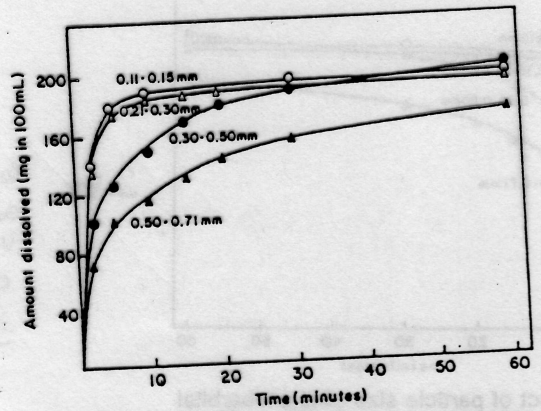



**Fig 4-8b.** Effect of particle size of phenobarbital on dissolution rate of the drug from tablets, in diluted gastric juice (surface tension 40.5 dynes $cm^{-1}$, pH 1.50). [Reproduced from Solvang and Finholt, *J Pharm Sci*, *59*, 51 **(1970).**]