DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 10(1), 137-156 (1984)



# DISSOLUTION OF SUPPOSITORIES IV: EFFECT OF CROSPOVIDONE ON ASPIRIN RELEASE FROM PEG BASES

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Previous reports from this laboratory have described a suppository dissolution test apparatus as well as the use of crospovidone to increase rate of release of acetaminophen from PEG suppositories. Also in previous reports from this lab, aspirin has been shown to give slow release from PEG bases and it was posited that addition of crospovidone to aspirin suppositories would also increase the rate of release. To test this hypothesis, four PEG blends were used as bases as in the previous studies. Each contained 350 mg of aspirin and 0.5%, 1%, or 5% of crospovidone (Polyplasdone XL, GAF). One thousand milliliters of phosphate buffer of pH 8.0 to approximately rectal pH was used as the dissolution media and maintained at 37.5°. A constant agitation rates of 25, and 50 rpm were used. Aspirin was assayed spectrophotometrically at 265 nm after appropriate dilution. Comparative dissolution profiles of the various agitation rates and with the concentrations of crospovidone were developed. Addition of crospovidone increased the dissolution rate constant and decreased dissolution half-times at the agitation rates. While the disintegration aide increased release, this release was not linear with respect to disintegrating agent concentration.

A recent report by Palmieri, et. al. (1) discussed the effect of crospovidone on release from PEG based suppositories of acetaminophen. Crospovidone, a commonly used disintegrating agent used in tablet manufacture, decreased the dissolution $t_{50}$'s for all bases studied. A previous report from the same



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laboratory reported that PEG based aspirin suppositories gave slow, unacceptable dissolution rates (2). This presentation reports the results of the effect of crospovidone on release of aspirin from PEG based suppositories.

## Preparation of Suppositories

Four basic formulas were used:

| | | |
|---|---|---|
| Base A | PEG 1000 | 96% |
| | PEG 4000 | 4% |
| | Aspirin | 350 mg |
| Base B | PEG 1000 | 75% |
| | PEG 4000 | 25% |
| | Aspirin | 350 mg |
| Base C | PEG 1540 | 70% |
| | PEG 6000 | 30% |
| | Aspirin | 350 mg |
| Base D | PEG 6000 | 50% |
| | PEG 1540 | 50% |
| | Aspirin | 350 mg |

Polyplasdone XL$^{R}$ was employed in concentrations of 0.5%, 1%, and 5% w/w.

The suppositories were prepared by fusion using a standard Armstrong 12 cavity aluminum alloy suppository mold.

## DISSOLUTION PROCEDURE

A suppository was positioned upright in the basket for suppository dissolution testing, previously described (2) and placed in a USP vessel containing 1000 mls of phosphate buffer pH 8.0 dissolution media to approximate the rectal pH. A Hanson dissolution drive control and hollow spindle-stirrer apparatus

was used to control the stirring rate at 25 rpm and 50 rpm. A constant temperature water bath was maintained at 37.5°.

Samples were withdrawn with a pipette fitted with glass wool plug to insure that undissolved drug was not withdrawn. An equivalent amount of fresh buffer was added to the flask after each withdrawal. After appropriate dilution the samples were assayed spectrophotmetrically at 265 nm for dissolved aspirin. The various PEG bases exhibited no absorption at that wavelength. Polyplasdone XL$^{R}$ also exhibited no absorption at this wavelength. Aspirin obeyed Lambert-Beer's Law at 265 nm,

Table 1

Base A Dissolution at 25 rpm

| Time (minutes) | % Release Aspirin 0%* | 1/2%* | 1%* | 5%* |
|---|---|---|---|---|
| 1 | 2 | 2 | 5 | 5 |
| 3 | 6 | 8 | 17 | 10 |
| 5 | 13 | 15 | 25 | 18 |
| 10 | 28 | 29 | 45 | 36 |
| 20 | 61 | 58 | 78 | 77 |
| 30 | 75 | 76 | 83 | 88 |
| 45 | 78 | 79 | 93 | 95 |

average of 5 assays

* = percentage of crospovidone

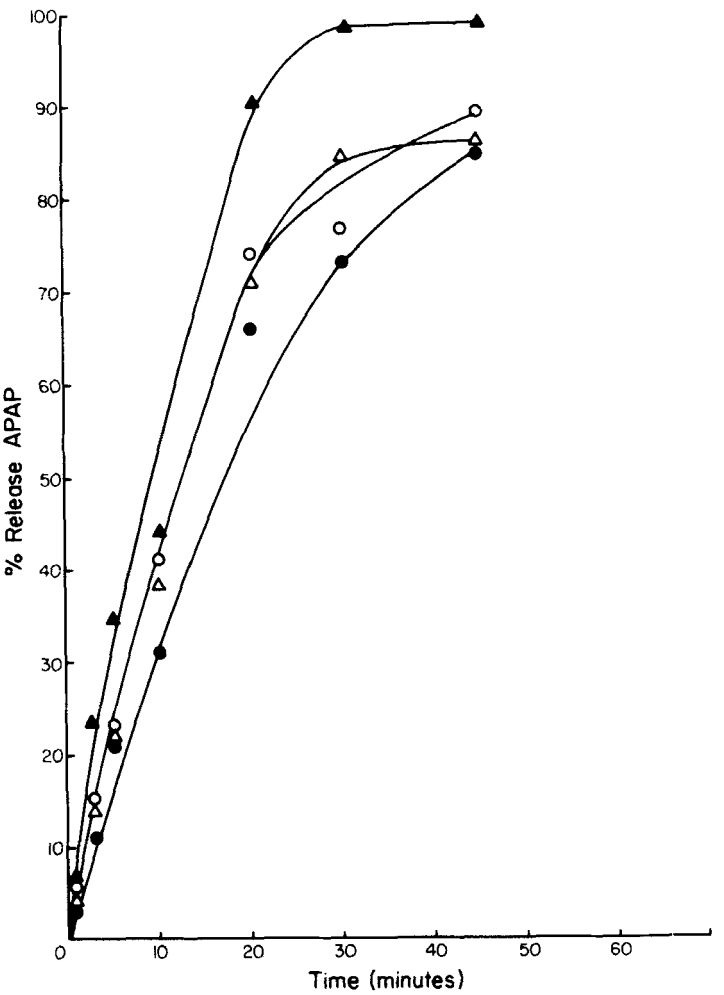


Figure 1: Dissolution profile for aspirin from Base A at 25 rpm with various percents of crospovidone

△ = 0% crospovidone

○ = 1/2% crospovidone

● = 1% cropsovidone

□ = 5% crospovidone

Table 2

Base A Dissolution at 50 rpm

| Time (minutes) | % Release Aspirin 0%* | 1/2%* | 1%* | 5%* |
|---|---|---|---|---|
| 1 | 5 | 4 | 5 | 5 |
| 3 | 10 | 12 | 16 | 11 |
| 5 | 18 | 30 | 33 | 17 |
| 10 | 50 | 49 | 60 | 41 |
| 20 | 68 | 78 | 88 | 76 |
| 30 | 73 | 80 | 92 | 87 |

average of 5 assays

* = percentage of crospovidone

the wavelength of maximum absorption for the drug and dissolved aspirn was calculated in this manner.

## RESULTS

Table 1 summarizes the data for release of aspirin from Base A with 0, 1/2, 1 and 5% polyplasdone at 25 rpm and this is shown graphically as Figure 1. Table 2 and Figure 2 present similar data at 50 rpm. Table 9 presents the dissolution half-times for the experiment with Base A. The addition of crospovidone at 1% concentration increased the dissolution $t_{50}$

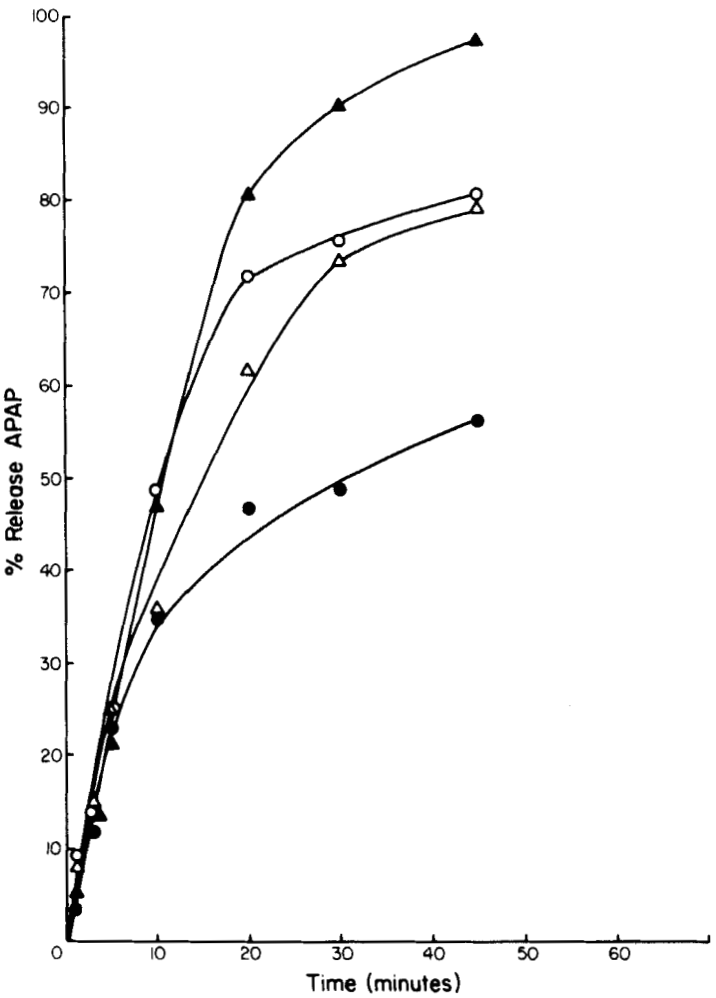


Figure 2: Dissolution profile for aspirin from Base A at 50 rpm with various percents of crospovidone

△ = 0% crospovidone

○ = 1/2% crospovidone

● = 1% cropsovidone

□ = 5% crospovidone

Table 3

Base B Dissolution at 25 rpm

| Time (minutes) | % Release Aspirin 0%* | 1/2%* | 1%* | 5%* |
|---|---|---|---|---|
| 1 | 1 | 2 | 2 | 3 |
| 3 | 12 | 13 | 5 | 10 |
| 5 | 17 | 17 | 12 | 18 |
| 10 | 36 | 35 | 29 | 41 |
| 20 | 65 | 66 | 65 | 71 |
| 30 | 78 | 78 | 75 | 88 |
| 45 | 81 | 80 | 81 | 93 |

average of 5 assays

* = percentage of crospovidone

Table 4

Base B Dissolution at 50 rpm

| Time (minutes) | % Release Aspirin 0%* | 1/2%* | 1%* | 5%* |
|---|---|---|---|---|
| 1 | 1 | 1 | 5 | 0 |
| 3 | 8 | 11 | 14 | 8 |
| 5 | 15 | 19 | 25 | 21 |
| 10 | 33 | 40 | 49 | 41 |
| 20 | 64 | 75 | 89 | 78 |
| 30 | 75 | 79 | 95 | 93 |

average of 5 assays

* = percentage of crospovidone

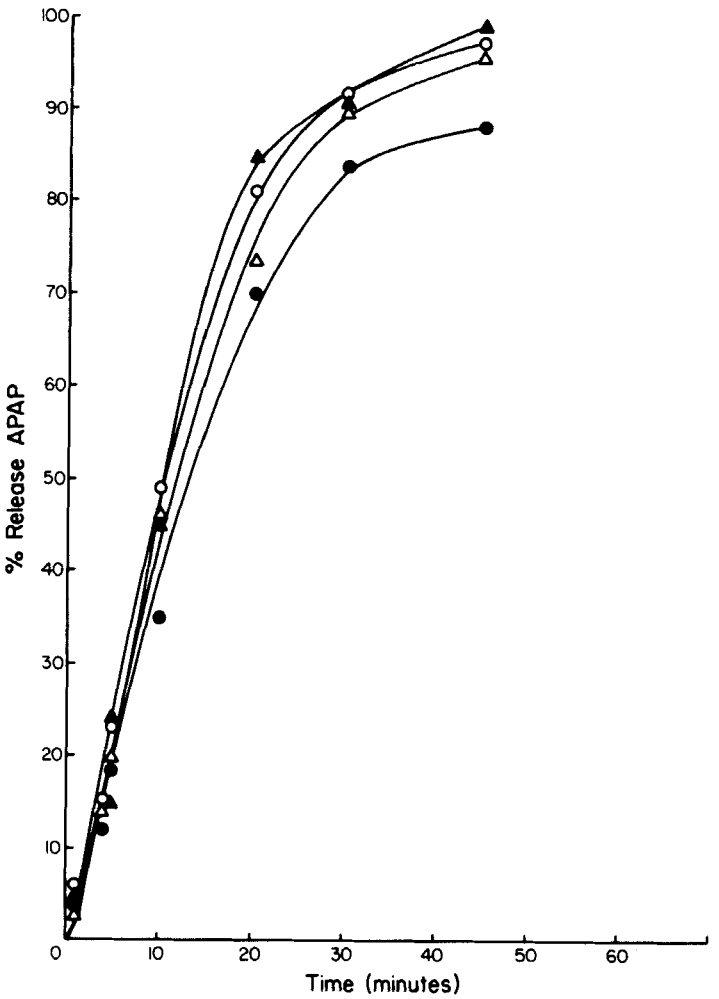


Figure 3: Dissolution profile for aspirin from Base B at 25 rpm with various percents of crospovidone

△ = 0% crospovidone

○ = 1/2% crospovidone

● = 1% cropsovidone

□ = 5% crospovidone

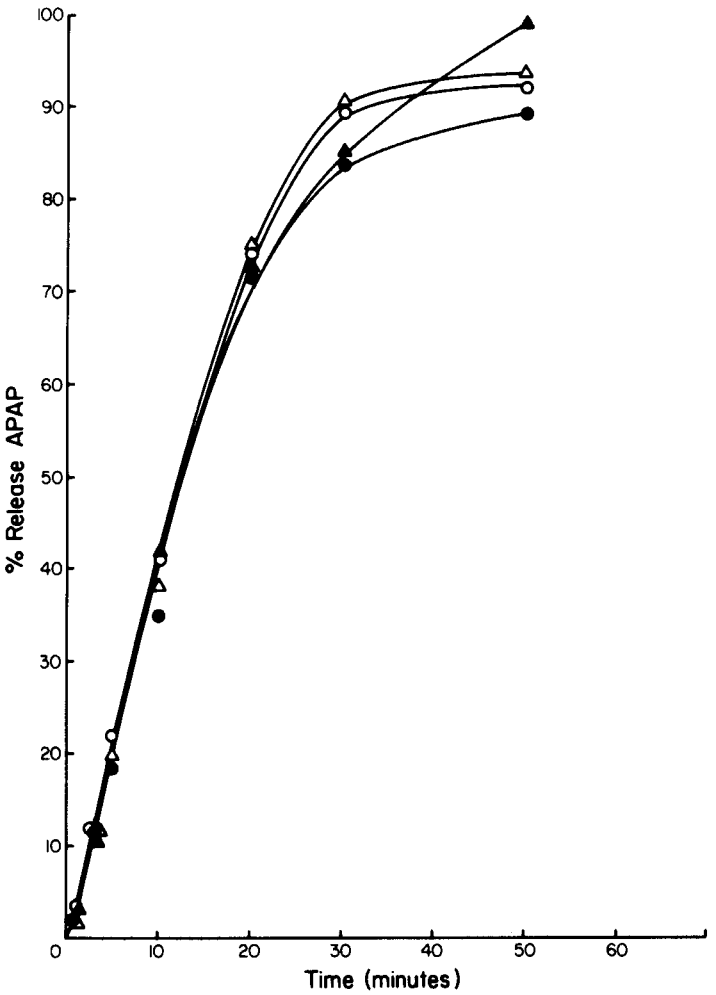


Figure 4: Dissolution profile for aspirin from Base B at 50 rpm with various percents of crospovidone

△ = 0% crospovidone

○ = 1/2% crospovidone

● = 1% cropsovidone

□ = 5% crospovidone

Table 5

Base C Dissolution at 25 rpm

| Time (minutes) | % Release Aspirin 0%* | 1/2%* | 1%* | 5%* |
|---|---|---|---|---|
| 1 | 2 | 2 | 5 | 2 |
| 3 | 6 | 6 | 12 | 7 |
| 5 | 12 | 9 | 14 | 10 |
| 10 | 24 | 23 | 32 | 21 |
| 20 | 46 | 44 | 45 | 49 |
| 30 | 68 | 65 | 64 | 72 |
| 45 | 71 | 76 | 78 | 85 |
| 60 | 76 | 81 | 86 | 91 |

average of 5 assays

* = percentage of crospovidone

from ten minutes to 12.5 minutes. This is unexplainable at present and further experiments are necessary to determine if this is an anomaly or a real occurrence. It is posited that the crospovidone may interfere with the release of aspirin or chemically combines with the aspirin. Since this occurs at both agitation rates, and in all individual samples, it probably is a real occurrence.

Tables 3 and 4 and Figures 3 and 4 depict Base B data at 25 and 50 rpm. As seen in Table 10, the dissolution $t_{50}$'s are

Table 6

Base C Dissolution at 50 rpm

| Time (minutes) | % Release Aspirin 0%* | 1/2%* | 1%* | 5%* |
|---|---|---|---|---|
| 1 | 3 | 3 | 3 | 3 |
| 3 | 7 | 8 | 7 | 8 |
| 5 | 13 | 13 | 13 | 13 |
| 10 | 27 | 28 | 26 | 34 |
| 20 | 49 | 55 | 45 | 53 |
| 30 | 67 | 75 | 73 | 71 |
| 45 | 78 | 96 | 89 | 96 |
| 60 | 78 | 98 | -- | 90 |

average of 5 assays

* = percentage of crospovidone

reduced with all crospovidone additions at all agitation rates. Additionally, the total percent release is increased at the 45 minute time interval is increased significantly.

Tables 5 and 6 as well as Figures 5 and 6 represent Base C with the various crospovidone concentrations. Table 11 summarizes the dissolution half-times for Base C. Once again the total amount released at 45 minutes was increased as the crospovidone concentration increased.

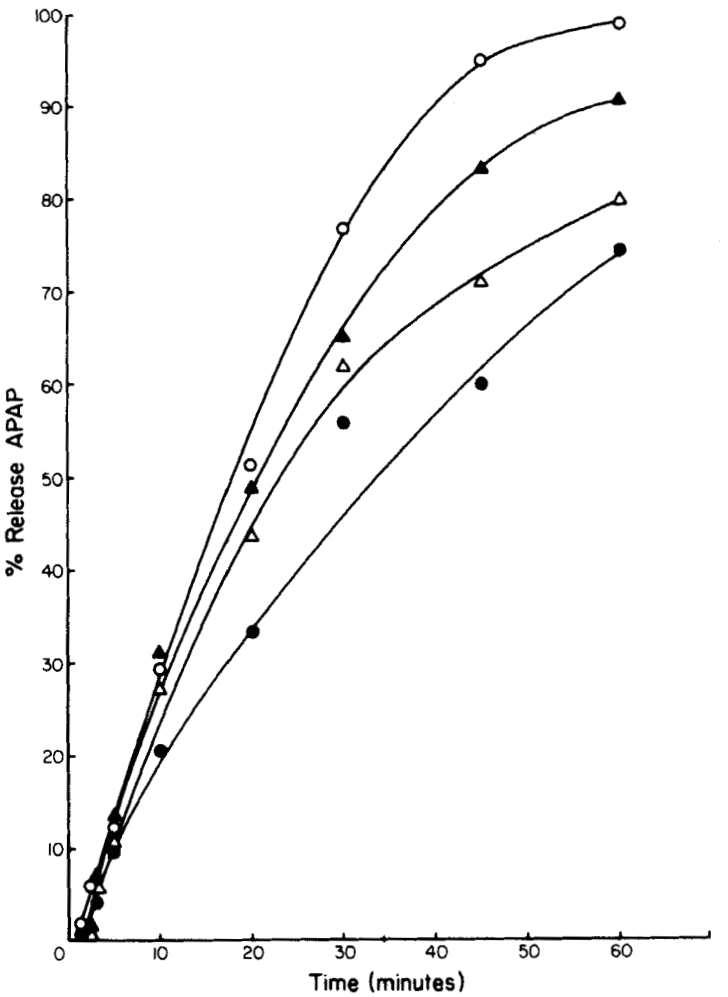


Figure 5: Dissolution profile for aspirin from Base C at 25 rpm with various percents of crospovidone

△ = 0% crospovidone

○ = 1/2% crospovidone

● = 1% cropsovidone

□ = 5% crospovidone

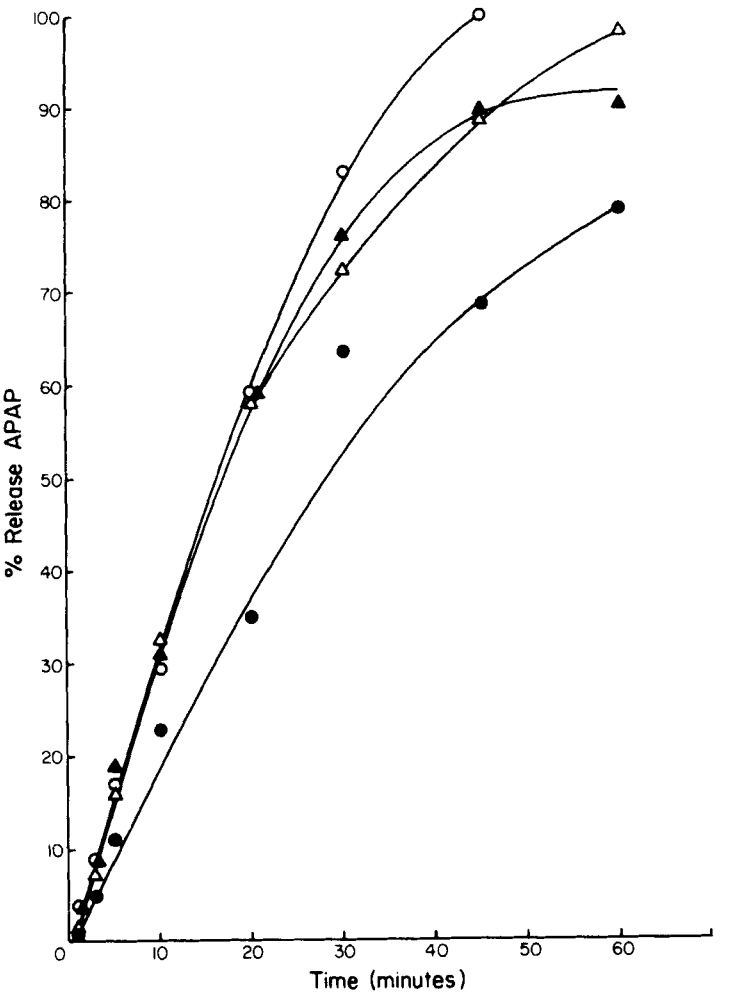


Figure 6: Dissolution profile for aspirin from Base C at 50 rpm with various percents of crospovidone

△ = 0% crospovidone

○ = 1/2% crospovidone

● = 1% cropsovidone

□ = 5% crospovidone

Table 7

Base D Dissolution at 25 rpm

| Time (minutes) | % Release Aspirin 0%* | 1/2%* | 1%* | 5%* |
|---|---|---|---|---|
| 1 | 2 | 2 | 0 | 2 |
| 3 | 4 | 5 | 5 | 4 |
| 5 | 8 | 12 | 8 | 9 |
| 10 | 18 | 20 | 22 | 21 |
| 20 | 38 | 41 | 45 | 36 |
| 30 | 56 | 58 | 69 | 55 |
| 45 | 76 | 78 | 90 | 80 |
| 60 | 81 | 82 | 96 | 85 |

average of 5 assays

* = percentage of crospovidone

Tables 7 and 8 along with Figures 7 and 8 present the various data for Base D and Table 12 summarizes the in vitro dissolution half-times. This data is inconclusive and similiar to that obtained for Base A since the 5% crospovidone did not decrease the dissolution half- times as expected. Possible explanations for this have been mentioned in discussion of the Base A results and further possible explanations will be investigated.

Table 8

Base D Dissolution at 50 rpm

| Time (minutes) | % Release Aspirin 0%* | 1/2%* | 1%* | 5%* |
|---|---|---|---|---|
| 1 | 2 | 2 | 2 | 2 |
| 3 | 6 | 7 | 8 | 6 |
| 5 | 9 | 12 | 14 | 9 |
| 10 | 23 | 21 | 20 | 23 |
| 20 | 46 | 44 | 43 | 46 |
| 30 | 63 | 64 | 61 | 67 |
| 45 | 87 | 88 | 87 | 89 |
| 60 | 91 | 93 | 91 | 96 |

average of 5 assays

* = percentage of crospovidone

## SUMMARY

When viewed with previously reported data for acetaminophen release from PEG-crospovidone suppositories, this data for aspirin does not offer as clean an explanation. However, the crospovidone did alter total release of acetaminophen in that there was a direct relationship of amount of crospovidone and percent aspirin release at 45 minutes. In many instances crospovidone addition did shorten the dissolution $t_{50}$.

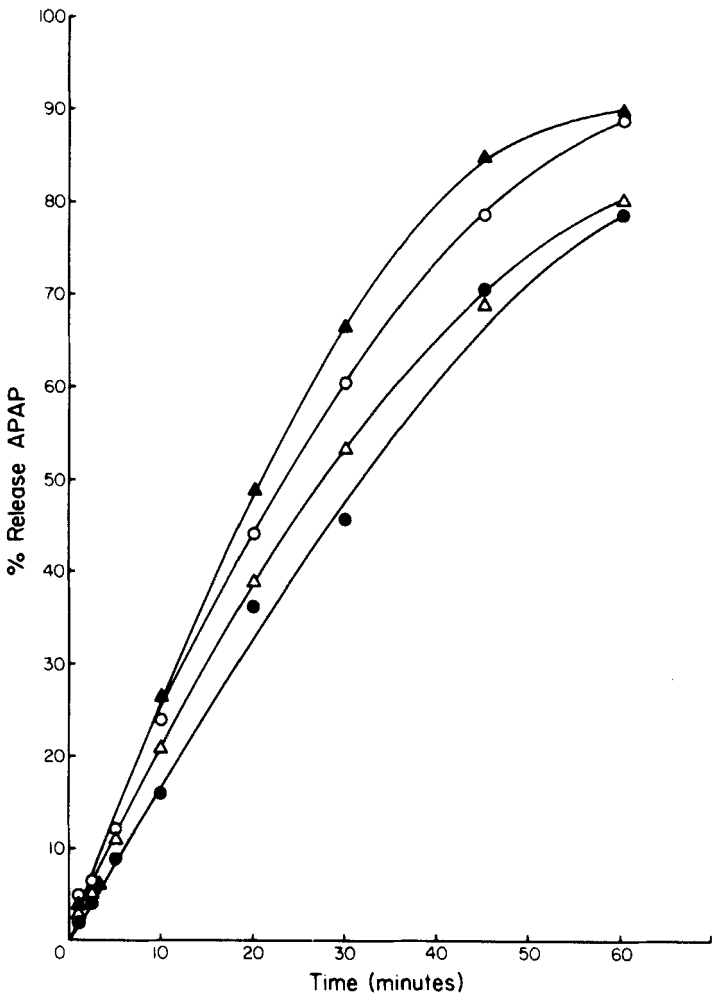


Figure 7: Dissolution profile for aspirin from Base D at 25 rpm with various percents of crospovidone

△ = 0% crospovidone

○ = 1/2% crospovidone

● = 1% cropsovidone

□ = 5% crospovidone

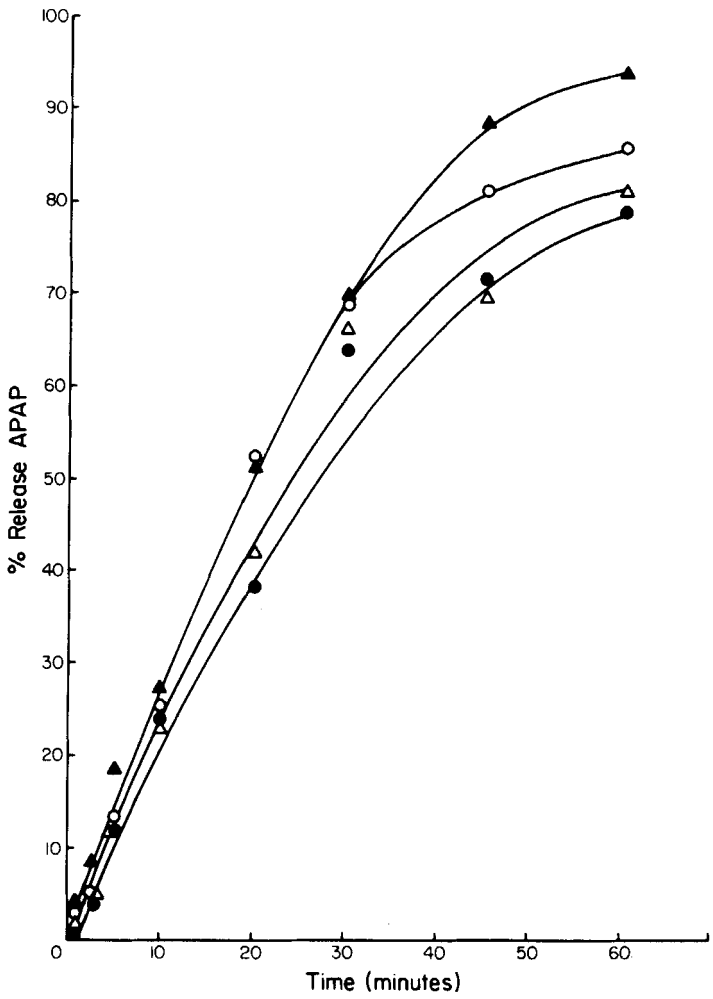


Figure 8: Dissolution profile for aspirin from Base D at 50 rpm with various percents of crospovidone

△ = 0% crospovidone

○ = 1/2% crospovidone

● = 1% cropsovidone

□ = 5% crospovidone

Table 9

Dissolution Half-times for Base A

| % crospovidone | 25 rpm (min) | 50 rpm (min) |
|---|---|---|
| 0 | 10 | 10 |
| 1/2 | 10 | 10 |
| 1 | 8 | 8 |
| 5 | 12.5 | 12 |

Table 10

Dissolution Half-times for Base B

| % crospovidone | 25 rpm (min) | 50 rpm (min) |
|---|---|---|
| 0 | 15 | 15.5 |
| 1/2 | 14 | 13 |
| 1 | 16 | 10 |
| 5 | 8 | 12 |

Table 11

Dissolution Half-times for Base C

| % crospovidone | 25 rpm (min) | 50 rpm (min) |
|---|---|---|
| 0 | 21.5 | 21 |
| 1/2 | 22 | 14 |
| 1 | 22.5 | 22 |
| 5 | 20.0 | 18 |

Table 12

Dissolution Half-times for Base A

| % crospovidone | 25 rpm (min) | 50 rpm (min) |
|---|---|---|
| 0 | 26 | 22.5 |
| 1/2 | 23 | 22.5 |
| 1 | 21 | 23 |
| 5 | 26 | 22.5 |

## References

1. Palmieri, A., Dissolution of Suppositories III: Effect of Crospovidone on Acetaminophen Release; Accepted for publication Drug Development and Industrial Pharmacy, to be published.

2. Palmieri, A., Drug Development & Industrial Pharmacy, 7:247 (1981).