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# SUPPOSITORY DISSOLUTION TESTING: APPARATUS DESIGN AND RELEASE OF ASPIRIN

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## ABSTRACT

Present methods of *in vitro* dissolution testing for suppositories were found to be lacking in universal acceptance, reproducibility, and difficult to perform. Initially a USP basket for tablet dissolution with one-hundred milliliters of phosphate buffer of pH 8 to approximate rectal pH was used. A slow constant stirring speed was maintained by means of a Hanson dissolution drive control and hollow spindle-stirrer apparatus as well as a constant temperature of 37.5±0.1°. Aspirin in polyethylene glycol bases gave plausible, reproducible results with this apparatus. However, oil bases (i.e. cocoa butter) gave unacceptable, irreproducible results since the base blocked the openings of the basket mesh. This report describes a modified basket method where the basket is polyurethane of the same size and con-

figuration as the USP basket. The basket described has twelve linear vertical slots of 0.25 mm width allowing for a porosity of 52%. Results of aspirin release from four PEG bases prepared in this laboratory are presented and discussed. The results were reproducible. Five commercially available suppositories were also tested in the above described manner.

Dissolution, or drug release has been extensively studied and reported for only a few selected tablets and other oral solid dosage forms. Dissolution has been shown to be the best *in vitro* parameter to correlate release of drug to bioavailability. Dissolution of drug from non-oral dose forms however, has not been extensively investigated. Past research into drug release from suppository bases has taken a number of approaches, some of which are not very scientifically sound or reproducible. Gibaldi and Gundhofer in 1975 studied bioavailability of aspirin from commercially available suppositories (1). These researchers reported "the rate of absorption of aspirin was sufficiently slow to raise considerable doubt as to whether efficaceous body levels of aspirin or salicylate are obtained after a single dose" (1). Other reports also question the absorption of aspirin from suppositories (2, 3).

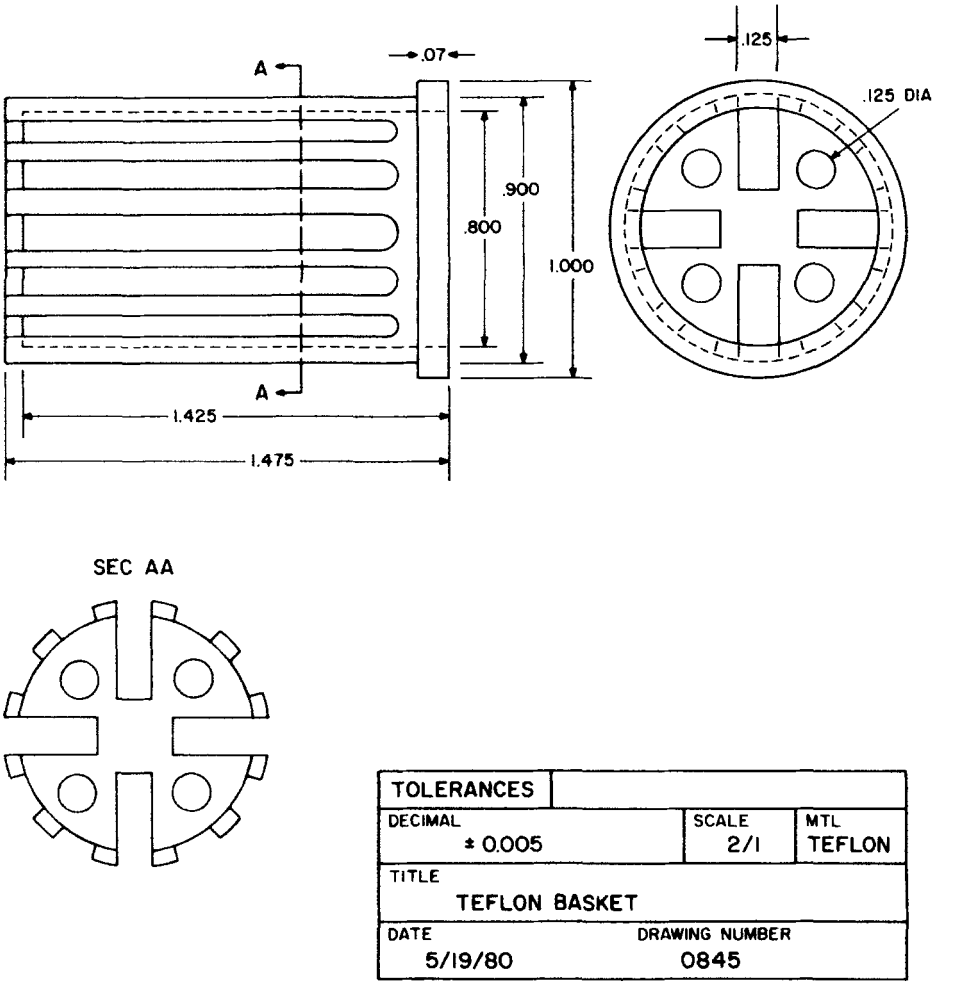
Because present methods of *in vitro* dissolution testing appeared lacking in universal acceptance and reproducibility

or were difficult to perform, this study was undertaken to develop an apparatus for suppository dissolution. To test the reproducibility of the devised method, four PEG base blends were used as vehicle for aspirin. Several commercially available products were also tested to determine their release patterns.

## EXPERIMENTAL

I. Design of Apparatus: Initially a USP basket for tablet dissolution was employed. However the suppository base, especially the cocoa butter, clogged the mesh in the basket and hindered free flow of dissolution media. Because of this a modified basket made from a teflon cylinder was fabricated (see schematic I). The polyurethane basket is of the same external dimensions as the USP basket and has twelve linear slots of 0.25 mm allowing for a porosity of 52%.

II. Dissolution Procedure: A suppository was positioned upright in the above described basket and placed in a modified Levy beaker containing 100 mls of phosphate buffer pH 8 dissolution media to approximate the rectal pH. A Hanson dissolution drive control and hollow spindle-stirrer apparatus was used to control the stirring at 50 and 100 rpm. A




Schematic I: Blueprint of Suppository Basket

constant temperature water bath was maintained at 37.5°.

Samples were withdrawn with a pipette fitted with glass wool plugs to insure that undissolved drug was not withdrawn. An equivalent amount of fresh buffer was added to the flask after each withdrawal. The samples were then assayed spectrophotometrically at 265 nm for dissolved aspirin. PEG bases exhibited no absorption at that wavelength.

III. Preparation of Suppositories

Four basic formulas were used:

| | | |
|---|---|---|
| Base A | PEG 1000 | 96% |
| | PEG 4000 | 4% |
| | ASA | 325 mg |
| Base B | PEG 1000 | 75% |
| | PEG 4000 | 25% |
| | ASA | 325 mg |
| Base C | PEG 1540 | 70% |
| | PEG 6000 | 30% |
| | ASA | 325 mg |
| Base D | PEG 6000 | 50% |
| | PEG 1540 | 50% |
| | ASA | 325 mg |

The suppositores were prepared by fusion using an Armstrong 12 cavity aluminum alloy suppository mold.

All commercial suppositories were purchased from local pharmacies.

## RESULTS AND DISCUSSION

Dissolution rate profiles were obtained as explained in the Experimental section.

The dissolution data for polyethylene glycol suppositories prepared in the lab and stirred at 100 rpm is shown in Table I while the 50 rpm data is tabulated as Table II.

As seen from these tables, Base B dissolved most quickly when agitated at 100 rpm, followed in order by base, A, C and D. At 50 rpm Base A dissolved most quickly

TABLE I: Dissolution of ASA Suppositories at 100 rpm[1]

| Time (min) | % of 325 mg ASA released: | | | |
|---|---|---|---|---|
| | Base A | Base B | Base C | Base D |
| 1 | 5 | 7 | 3 | 3 |
| 2 | 12 | 18 | 5 | 8 |
| 5 | 32 | 30 | 17 | 17 |
| 10 | 58 | 41 | 36 | 44 |
| 15 | 73 | 60 | 50 | 59 |
| 20 | 80 | 74 | 64 | 65 |
| 25 | 80 | 80 | 76 | 68 |
| 30 | 86 | 82 | 78 | 71 |
| 40 | 85 | 85 | 82 | 72 |
| 50 | 85 | 90 | 83 | 73 |
| 60 | 83 | 90 | 82 | 73 |

[1] average of 20 assays

TABLE II: Dissolution of ASA Suppositories at 50 rpm[1]

| Time (min) | % of 325 mg ASA released: | | | |
|---|---|---|---|---|
| | Base A | Base B | Base C | Base D |
| 1 | 10 | 3 | 2 | 2 |
| 2 | 28 | 7 | 5 | 3 |
| 5 | 53 | 16 | 12 | 10 |
| 10 | 60 | 32 | 26 | 23 |
| 15 | 68 | 50 | 36 | 37 |
| 20 | 85 | 65 | 44 | 47 |
| 25 | 85 | 70 | 52 | 53 |
| 30 | 85 | 70 | 52 | 53 |
| 40 | 85 | 73 | 69 | 69 |
| 50 | 85 | 72 | 68 | 73 |
| 60 | 85 | 73 | 69 | 74 |
| 70 | 85 | 73 | 68 | 73 |
| 80 | 85 | 73 | 69 | 74 |
| 90 | 85 | 73 | 68 | 73 |

[1]average of 20 assays

followed by B, C and D. These data are graphically presented in Figure 1 and 2. From Figure 1 and 2, the dissolution half-times of $t_{50}$'s are calculated and reported in Table III. From these data it appears that Base A has the fastest $t_{50}$.

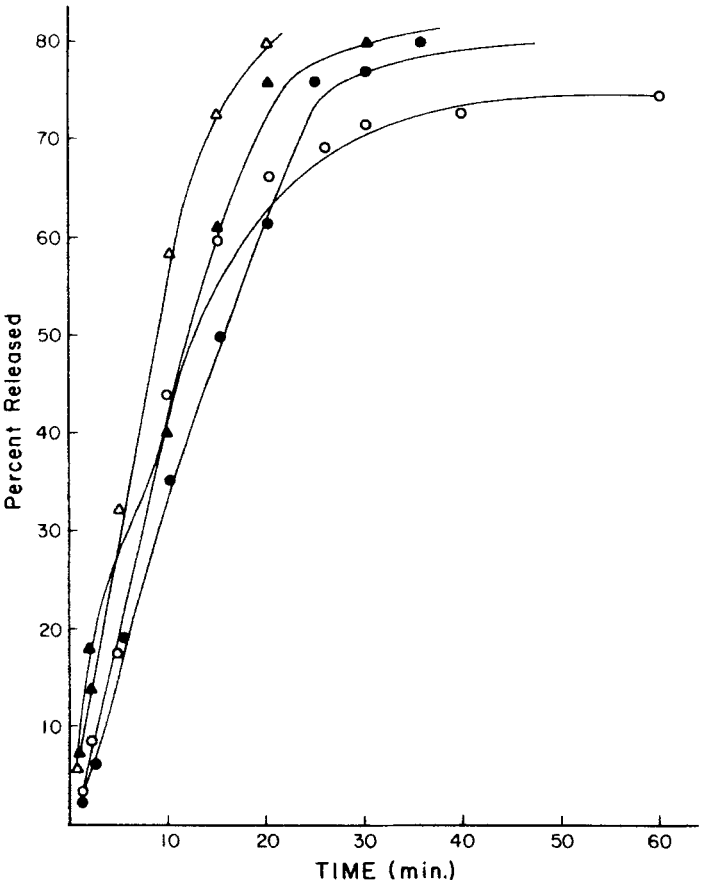



Figure 1: Release of Aspirin from PEG bases at 100 rpm.

Key △ Base A ○ Base C

▲ Base B ● Base D

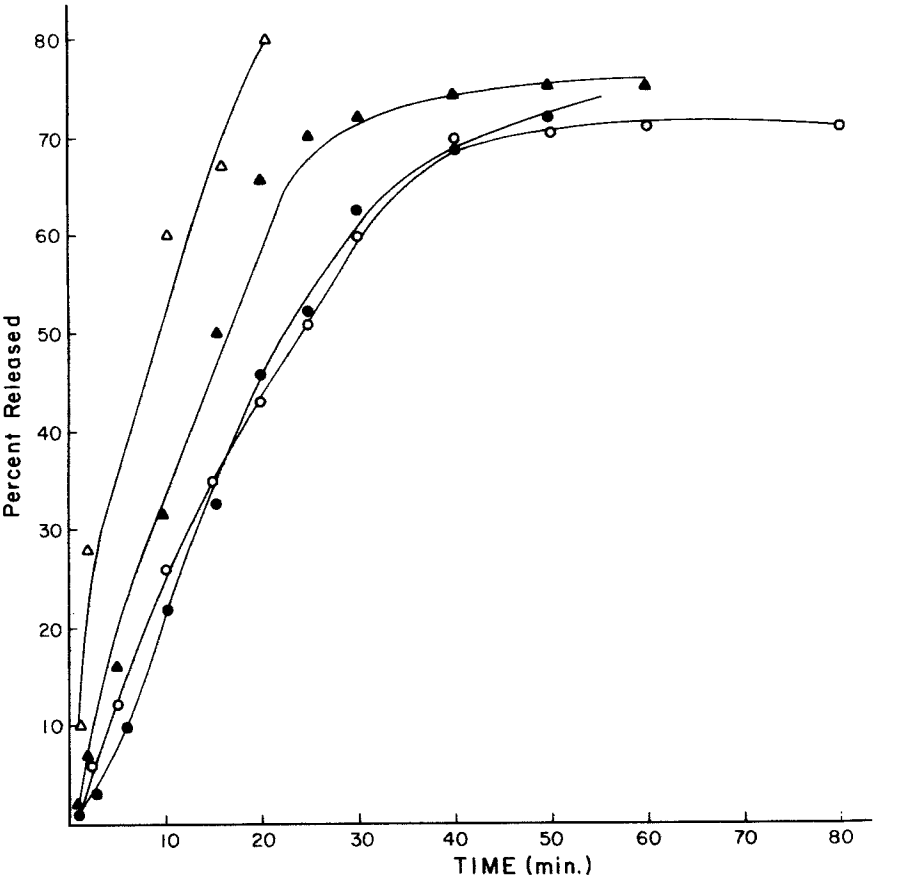



Figure 2: Release of Aspirin from PEG bases at 50 rpm.

Key △ Base A ○ Base C

▲ Base B ● Base D

TABLE III: Dissolution half-times for ASA release from PEG Bases

| Base | $t_{50}$ at 100 rpm (min) | $t_{50}$ at 50 rpm (min) |
|---|---|---|
| A | 9 | 9 |
| B | 12 | 16 |
| C | 16 | 25 |
| D | 12 | 23 |

The dissolution profiles obtained at the slower agitation rate appear more discriminating and as such, should be accepted as the method of choice for the dissolution testing of suppositories.

Commercially available products were subjected to similar experimentation. These results are shown in Table IV and Figure 3. Comparing these findings with the laboratory PEG bases, the dissolution of the commercially available products is considerably slower and the total amount released at any time is significantly less. Obviously, these bases were of a slightly different nature and of an undetermined formula. All of these suppositores had a "feel" and appearance similar to the PEG bases prepared in the laboratory. Due to previous experience with companies not render-

TABLE IV: Dissolution Data for Commercially Available Aspirin Suppositories at 100 rpm[1]

| Time (min) | A (325 mg) | B (325 mg) | C (325 mg) | C (60 mg) | C (125 mg) |
|---|---|---|---|---|---|
| 1 | 0.7 | 0.8 | 0.8 | 5.7 | 0.5 |
| 5 | 1.3 | 2.1 | 1.9 | 11.4 | 2.0 |
| 10 | 1.9 | 2.6 | 2.4 | 13.2 | 3.5 |
| 20 | 3.2 | 3.4 | 4.7 | 15.9 | 5.4 |
| 30 | 7.8 | 4.2 | 15.2 | 18.5 | 7.5 |
| 40 | 8.8 | 4.3 | 18.3 | 20.2 | 8.9 |
| 50 | 10.6 | 4.3 | 29.9 | 21.2 | 9.7 |
| 60 | 11.1 | 15.5 | 20.6 | 21.3 | 9.7 |
| 70 | 12.8 | 5.7 | 21.7 | -- | -- |
| 80 | 12.2 | 8.1 | 23.5 | -- | -- |
| 90 | 13.1 | 9.3 | 27.6 | -- | -- |

[1]average of 20 assays

ing this type of information, the manufacturers of these suppositories were not contacted as to the exact formulation ingredients in their bases.

All of the commercially available suppositores were labeled "Aspirin U.S.P." and in all probability met U.S.P. standards. The results indicate that the base is critical in release of aspirin from the suppository. The official compendium does not designate a specific base. Future communications will report *in vivo* - *in vitro* correlations.

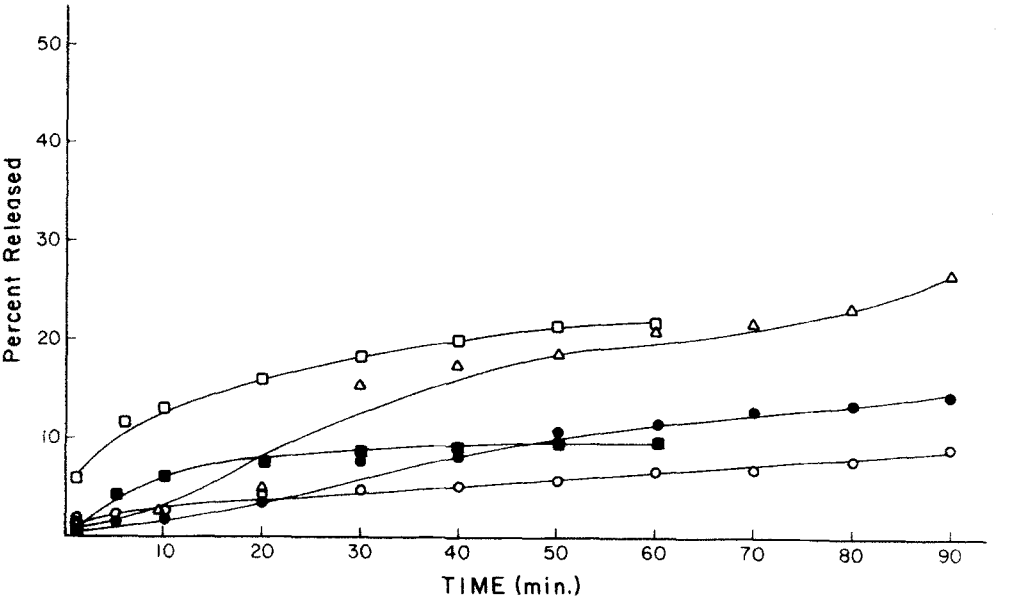



Figure 3: Release of Aspirin from Commercially Available Suppositories.

Key

- ● Brand A (325 mg)
- ○ Brand B (325 mg)
- □ Brand C (60 mg)
- ■ Brand C (125 mg)
- △ Brand C (325 mg)

## CONCLUSIONS

1. A new apparatus design has been offered for suppository dissolution.
2. This apparatus gives reproducible data.
3. Aspirin in PEG bases prepared in the laboratory have $t_{50}$ times that relate to the specific PEG's employed.
4. Commercially available aspirin has unsatisfactory dissolution, possibly indicating poor bioavailability.
5. From these preliminary results, it can be posited that the suppository base is critical in drug release and the base should be specified in the official compendia.

## REFERENCES

1. Gibaldi, M. and Grundhofer, J., J. Pharm. Sci., 64:1064 (June 1975)
2. Lowenthal, W. Borzelleca, J.F., and Corder, C.D., Jr., J. Pharm. Sci., 59:1353 (September, 1970).
3. Parrott, E.L., J. Pharm. Sci., 60:867 (June 1971).