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Research Papers

Some geometrical considerations concerning the design of tablets

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A theoretical examination of designs best suited to give a uniform rate of release of materials from solution tablets is presented.

THERE are circumstances in medical and industrial practice where solid material in the form of tablets has to pass into solution rather than to disintegrate. In certain circumstances it is desirable that the material should be released at a uniform rate. The purpose of this paper is to examine the theoretical considerations which underly the choice of a design to achieve this object.

Let a tablet be immersed in a fluid: consider a small region ABCD of area Δs on the surface of the tablet (Fig. 1). In a small interval of time

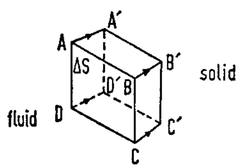

FIG. 1.

Δt a volume $\sigma\Delta s\ \Delta t$ of the tablet in the form of a layer ABCDA'B'C'D', where $AA' = BB' = CC' = DD' = \sigma\Delta t$(AA', BB', CC', DD' perpendicular to the plane ABCD) will pass into solution. It will be assumed that σ is a constant. This will be (approximately) so if the material of the tablet is of uniform composition and if certain obvious conditions on the solubility and rate of diffusion and on the relative volumes of tablet and fluid are met. Consider, then a tablet in the form of a parallelipiped, ABCDA'B'C'D' (Fig. 2) with $CD = DD' = l$, $AD = m$.

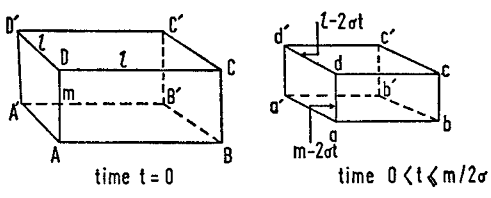

FIG. 2.

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From the preceding considerations we infer that in any interval Δt (preceding the tablet's final disappearance) each dimension of the tablet is reduced by a length $2\sigma\Delta t$. Hence, if the tablet is placed in fluid at time $t = 0$, at time t it will be reduced to the parallelipiped abcda'b'c'd' (Fig. 2) where $aa' = AA' - 2\sigma t$, $ab = AB - 2\sigma t, \ldots$ Hence, supposing $m \leqslant l$, the tablet will be completely dissolved when $m - 2\sigma t = 0$, i.e. at time $\tau = m/2\sigma$. So by computing surface areas we find that the rate of solution $\Sigma(t)$ at time t, for $t < \tau$, is given by

$$\Sigma(t) = \sigma.2l(2m + l) - 8\sigma^2 t(m + 2l) + 24\sigma^3 t^2 \quad \ldots \quad (1)$$

Fig. 3 shows the graph of $\Sigma(t)$.

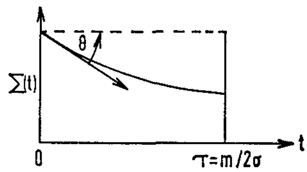

FIG. 3. Time variation of rate of solution.

The noteworthy feature here is that the rate of solution initially drops, the tangent to the curve at $t = 0$ being inclined at an angle θ to the t-axis, where $\tan\theta = 8\sigma^2 (m + 2l)$ = coefficient of t in $\Sigma(t)$. Further it is clear that no adjustment of dimensions of the tablet (short of putting $m = l = 0$!) can make $\theta = 0$. The mathematical problem we face can now be defined. For a given tablet, let $\Sigma(t)$ denote the rate of solution at time t after first being immersed in fluid and let τ denote the time at which the tablet is first completely dissolved. Assume that $\Sigma(t)$ can be expanded in the form

$$\Sigma(t) = \Sigma(0) + A_1 t + \phi(t) \quad \ldots \quad \ldots \quad (2)$$

where *$\phi(t) = a_0 t^2 + a_1 t^3 + \ldots$. The constant A_1 represents the initial rate of fall of $\Sigma(t)$, i.e. $\tan\theta = \frac{d\Sigma}{dt_{t=0}} = A_1$. In general A_1 is a function of the initial size of the tablet [c.f. (1)]. Thus our problem is to define some shapes of tablet for which $A_1 = 0$: then for such shapes

$$\Sigma(t) = \Sigma(0) + \phi(t), \ \phi(t) = a_0 t^2 + a_1 t^3 + \quad \ldots \quad (3)$$

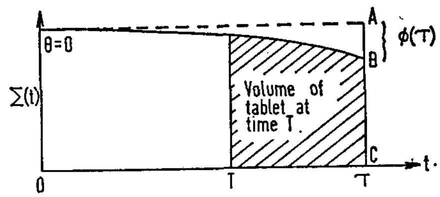

FIG. 4. Rate of solution of crs-tablets.

* Note $\int_0^\tau \Sigma(t)dt$ = initial volume of tablet = area under graph of $\Sigma(t)$.

Tablets having such a shape we call *crs-tablets*: the graphs of their rate of solution have the form shown in Fig. 4. Of course, in general, the rate of change of $\Sigma(t)$, even for crs-tablets is non-zero because of the term $\phi(t)$ in (3). Hence as a measure of efficiency, ϵ, of a crs-tablet we take the proportionate drop in the rate of solution when the tablet is finally dissolved, i.e. referring to Fig. 4.

$$\epsilon = \frac{BA}{CA} = \frac{\Sigma(0) - \Sigma(\tau)}{\Sigma(0)} = \frac{\phi(\tau)}{\Sigma(0)} \quad \cdots \quad \cdots \quad (4)$$

Thus to get $\Sigma(t)$ as nearly constant as possible in a crs-tablet we aim, by adjusting the dimensions of the tablet, to make ϵ as small as possible.

The tablet shown in Fig. 2 is a non crs-tablet because the surface area decreases as the tablet dissolves. Our plan is to compensate for this decrease by incorporating in the tablet a surface whose area increases. Consider a cylindrical hole in a tablet (Fig. 5). If the hole has radius r

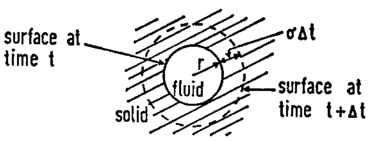

FIG. 5

at time t, then by the assumptions of the second paragraph, the radius will increase to $r + \sigma\Delta t$ at $t + \Delta t$. Hence the surface area of the hole will increase. We shall therefore consider tablets with holes in them: by appropriate choice of dimensions the tablets can be given the desired property.

Crs-tablets

In order to minimise computational complexity in finding surface areas we consider only tablets in the form of parallelipipeds.

1. One hole tablets (Fig. 6).

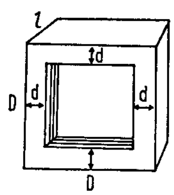

FIG. 6

Suppose $l \leqslant d$. Then $\tau = d/2\sigma$ and

$$\Sigma(0) = 8(l + d)(D - d)\sigma$$

$$\Sigma(t) = \Sigma(0) + 32\sigma^2 (d - D)t \text{ for } 0 \leqslant t \leqslant \tau \quad \cdots \quad (5)$$

(In this instance $\phi(t) = 0$, though this is not the case with the following examples). Now $D \geqslant 2d$. So comparing (5) and (2) we have $A_1 = 32\sigma^2 (d - D) < 0$. Thus a one-hole tablet of this type cannot be a crs-tablet.

2. Two hole tablets (Fig. 7).

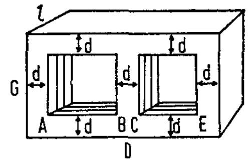

FIG. 7

Suppose $l \geqslant d$, AB = CE. Then $D \geqslant 3d$, $G \geqslant 2d$, $\tau = d/2\sigma$.
Thus

$$\Sigma(0) = 2\sigma[l(3G + 2D - 7d) + d(3G + 2D - 6d)]$$

$$\Sigma(t) = \Sigma(0) - 8\sigma^2(3G + 2D - l - 7d)t + 24\sigma^3t^2 \text{ if } 0 \leqslant t \leqslant \tau \qquad (6)$$

Comparing (3) and (6) it can be seen that we can construct a crs-tablet by choosing

$$3G + 2D = l + 7d \quad .. \quad .. \quad .. \qquad (7)$$

The efficiency, by (4) is then, using (7),

$$\epsilon = 3d^2/[(3G + 2D - 7d)^2 + d(3G + 2d - 6d)] \quad .. \qquad (8)$$

Examples:

(i) $D = 5d$, $G = 3d$. By (7), $l = 12d$; (8) gives $\epsilon \cong \frac{1}{52}$.

(ii) $D = 7d$, $G = 3d$. Then $l = 16d$ and $\epsilon \cong \frac{1}{90}$.

Further information can be extracted from (8). In fact we can construct an upper bound for ϵ. Define μ by $(3G + 7d)/d = 12 + \mu$. Then since $D \geqslant 3d$, $G \geqslant 2d$ we have $\mu \geqslant 0$. Further, (8) can be rewritten as

$$\mu^2 + 11\mu + (31 - 3/\epsilon) = 0 \quad .. \quad .. \qquad (9)$$

The condition $\mu \geqslant 0$ requires that (9) have one positive solution.

Thus $$0 < \epsilon \leqslant 3/31,$$

i.e. it is impossible to get the efficiency worse than 3/31. For any ϵ such that $0 < \epsilon \leqslant 3/31$ a positive μ can be computed from (9) and hence G, D and l can be found.

3. Three-hole tablets (Fig. 8).

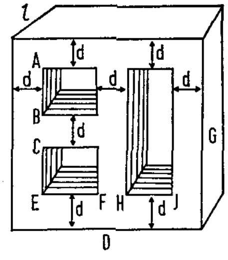

FIG. 8

Suppose $l \geqslant d$, AB = CE, EF = HJ. Then $G \geqslant 3d$, $D \geqslant 3d$, $\tau = d/2\sigma$. Hence,

$$\Sigma(0) = \sigma[l(6G + 5D - 19d) + d(6G + 5D - 15d)]$$

$$\Sigma(t) = \Sigma(0) - 4\sigma^2(6G + 5D - 19d - 4l)t - 48\sigma^3t^2 \text{ for } 0 \leqslant t \leqslant \tau \quad (10)$$

By putting

$$6G + 5D = 4l + 19d \quad \ldots \quad (11)$$

in (10) we have a crs-tablet whose efficiency, by (4) and (11) is

$$\epsilon = 48d^2/[(6G + 5D - 19d)^2 + 4d(6G + 5D - 15d)] \quad (12)$$

Examples:

(i) $G = 5d$, $D = 5d$. By (11), $l = 9d$. By (12), $\epsilon \cong 1/33$.

(ii) $G = 5d$, $D = 7d$. Then $l = 23d/2$ so that $\epsilon \cong 1/48$.

Next, by imposing the conditions $G, D \geqslant 3d$ on (12) we get

$$0 < \epsilon \leqslant 12/77.$$

4. Four-hole tablet (Fig. 9).

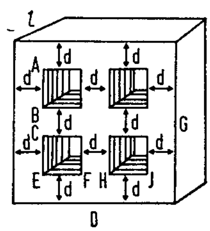

FIG. 9

Suppose $l \geqslant d$, AB = CE, EF = HJ. Then $D, G \geqslant 3d$, $\tau = d/2\sigma$.

$$\Sigma(0) = 6\sigma[l(D + G - 4d) + d(D + G - 3d)]$$

$$\Sigma(t) = \Sigma(0) - 24\sigma^2(D + G - 4d - l)t - 72\sigma^3t^2 \text{ for } 0 \leqslant t \leqslant \tau.$$

If

$$D + G = 4d + l$$

we have a crs-tablet whose efficiency is given by

$$\epsilon = 3d^2/[(D + G - 4d)^2 + d(D + G - 3d)] \quad \ldots \quad (13)$$

Examples:

(i) $G = 5d$, $D = 5d$; $l = 6d$ and $\epsilon \cong 1/14$.

(ii) $G = 7d$, $D = 5d$; $l = 8d$ and $\epsilon \cong 1/24$.

(iii) $G = 9d$, $D = 5d$; $l = 10d$ and $\epsilon \cong 1/36$.

Finally, the conditions $D, G \geqslant 3d$ and (13) require

$$0 < \epsilon \leqslant 3/7.$$

Conclusion

Crs-tablets can be constructed with two or more holes—a single hole is unable to compensate the decrease in the outer surface area. The 2, 3, 4-hole csr-tablets have a natural ratio above which the proportionate decrease in the rate of solution cannot rise; $\frac{3}{39}$, $\frac{12}{77}$, $\frac{3}{7}$ respectively. If we take these as figures of merit we see that the two-hole tablet is basically a better structure than the others.