



Private prescription:

A thought-provoking tonic on the lighter side

Column by Raymond C. Rowe, AstraZeneca, UK

Please note that these are the personal opinions of the author and do not necessarily represent those of AstraZeneca.

Powders, pills and controlled release: a doggerel's delight

A doggerel, to the uninitiated who, like me, had little literary education, is a trivial form of verse, loosely constructed and often irregular, but highly effective because of its simple mnemonic rhyme. Doggerels are a rich source of comedy and satire and often appear in nonsense verse, epitaphs and commercial jingles. I first stumbled across this form of verse when I was researching an editorial for *Drug Discovery Today*¹. Over the past few months, I have unearthed several more with connotations and associations with pharmaceutical science and technology, specifically oral dosage forms, providing a light-hearted, but thought-provoking, viewpoint of the subject.

Powders

Powders, especially effervescent powders, were an extremely popular preparation in the early part of the 20th century. The British Pharmaceutical Codex (BPC) of 1923, for example, contained 28 monographs for such preparations, including those for such potent drugs as acetanilide, phenacetin and quinine. These were often extemporaneously dispensed

in two parts; the first containing the drug mixed with either sodium bicarbonate or tartaric acid, and the second part with either tartaric acid or sodium bicarbonate. The idea was to dissolve the first part in a tumbler of water, add the second part, and drink while the preparation was effervescing. As nowadays, not all patients followed the instructions, as told in the epitaph of Mary Ann Lowder from Burlington (MA, USA)²:

Here lies the body of Mary Ann
Lowder,
She burst while drinking a seidlitz
powder,
Called from the world to her
heavenly rest,
She could have waited 'til it
effervesced.

For information, a seidlitz powder contained sodium potassium tartarate and was used as a saline purgative.

Pills

For centuries, pills provided a simple but rather crude method of delivering drugs

in unit doses convenient for the patient. Apart from their obvious ease of administration, they had the advantage of being readily prepared extemporaneously with simple equipment, regardless of whether or not the drug was a powder. Their popularity in the early part of the 20th century is shown by the fact that the BPC of 1923 contained 49 different pill monographs. Even in the 1950s, demand was such that the manufacturing process was mechanised for large scale production. One such preparation was Beecham's Pills, a formulation containing aloes and ginger, used as a purgative and manufactured by Beecham Products at St Helens, Lancashire, UK. An advertising jingle, devised but never used for the product, provides information on the dose³:

Hark! The herald angels sing!
Beecham's Pills are just the thing,
Two for a woman, one for a child.
Peace on earth and mercy mild!

This doggerel has been attributed to that great composer Sir Thomas Beecham (1879–1961), who is said to have composed it for his father, Sir Joseph Beecham (1820–1907), the founder of the company³.

Controlled release

The concept of oral controlled release has been around for many years and many technologies have been proposed, tried and tested. These range from tablets prepared using polyvinyl chloride that release the drug slowly through pores within the plastic matrix, to capsules containing hydrogel plugs that release the drug when the plug is ejected at a specified time after ingestion. Parallel to this has been the invention of probes that can monitor the pH of the gastrointestinal contents *in vivo*. Many scientists have proposed the concept of 'intelligent' systems that combine both of these elements and that would release their contents when and where the drug

was required. LeNore Stumpf foresaw this in 1969 (Ref. 4):

How is it that a little pill
Without a pair of eyes to see
Can travel down, and round and
round
And figure out what's wrong with
me?
I bet if I should get the gout,
The mumps, the measles or the flu
A pill could scurry in a hurry
And fix me up as good as new.

However, sophisticated technology can go wrong, as noted by Stumpf in the concluding part of the doggerel:

Supposing though I got a pill,
A pill that wasn't so compliant.
Then just to prove it needn't move
It might become downright defiant.
I couldn't cure my head or foot.
A cold could get the best of me
If a pill got chummy with my tummy
And just ignored the rest of me!

Manufacture and scale-up

The development of a formulated product intended for manufacture is not complete until the process is successfully proven on a large scale. Many formulations and processes are trouble free at the laboratory scale but show unsatisfactory features as soon as the scale of operation is increased, or, as so aptly put by Francis Freeth, an ICI director, in 1929 (Ref. 5):

First the test-tube, then the pail,
Then the semi-working scale,
Then the Plant, and then disaster –
Faster, faster, faster, faster!

Admittedly, this doggerel was composed specifically for chemical manufacture but it is directly relevant to pharmaceutical product manufacture, especially now with the need to reduce development costs and time scales by attempting scale-up at an earlier stage. If the scale-up is not carried out satisfactorily then 'faster can lead to disaster'.

A final word

As can be seen, doggerels can provide some interesting insights into oral dosage forms and their manufacture. There are probably many more around in the literature. Scientists should not be hesitant in committing their thoughts to paper in such a format. Science should be fun and the doggerel is a fun form of verse.

References

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