

How New Dosage Forms Prolong the Lifecycle of Mature Products



An age-old problem of the pharmaceutical industry is what to do if product sales are dropping or are anticipated to drop. How can you revitalise an ageing product, boost brand loyalty and recapture interest? One approach is to develop existing APIs into one or more alternative dosage forms. This article looks at the benefits of user-friendly dosage forms and what they offer to the pharmaceutical industry.

There are a number of reasons why an ageing product or brand may need a boost. Perhaps a product will soon come off patent and generic versions are anticipated to appear on the market. Alternatively, perhaps your OTC product is facing increased competition and is losing market share. Could reformulating your API into alternative dosage forms be the way to make your product more popular? Through adding further dosage forms, you could potentially build a product range that leverages existing brand loyalty, whilst better meeting the needs of end-users. Alternatively, it could be that reformulation offers the opportunity to combine one or more APIs or enable once-daily dosing, boosting the efficacy or convenience of a product.

Reformulation as a user-friendly dosage form could be the way forward...

What are User-friendly Dosage Forms?

User-friendly dosage forms are orally administered alternatives to conventional solid tablets and capsules. They include effervescent tablets, instant drinks, orally disintegrating granules, chewable tablets and lozenges. Whilst each form has its own distinct advantages, they share three common benefits for end-users: they are easy to swallow, convenient to take and are specially formulated to have a pleasant taste.

The Trouble with Tablets

Tablets and capsules have for many years been the standard method for patients to take medication. Yet solid tablets may be considered uncomfortable and even painful to swallow, depending on size, shape and surface texture. This can present a problem – even for people who do not ordinarily find

swallowing difficult. A recent survey conducted by HERMES PHARMA and the Spiegel Institut Mannheim found that, out of approximately 2000 people surveyed in the US and Germany, over half experienced difficulties swallowing tablets and capsule¹. What's more, these findings were not unique to a specific demographic, such as the elderly or infirm. Indeed, 70% of people under the age of 34 found swallowing solid tablets difficult – the highest of all the age groups studied. Frequently cited reasons include tablets being too large, getting stuck in the throat, or having an unpleasant taste or odour.

And it is not just swallowing that people dislike about tablets. With modern consumers and patients increasingly used to having choice and convenience in their lives, there exists a clear demand for dosage forms that come in a variety of flavours and are convenient to use 'on the go'. Amongst older users, difficulties associated with opening blister packaging are also a common complaint.

The survey also discovered that, in an effort to get around the difficulties associated with swallowing their medicine, many people modified their tablets by chewing them, breaking them up before swallowing or by dissolving them in water. Such actions change the way the formulation works, altering the API release profile and impacting on bioavailability and efficacy. Perhaps most worryingly, around one in ten surveyed resorted to not taking their medication at all.

Non-compliance not only presents risks to an individual's health, but the healthcare system as a whole. In the US, for instance, non-compliance is believed to cost the healthcare system as much as \$289 billion a year². It's clear, therefore, that the solution to this problem will undoubtedly win favour with healthcare experts and end-users alike.

How do User-friendly Dosage Forms Help Combat these Issues?

User-friendly dosage forms offer smart solutions to these challenges, whilst creating a convenient and enjoyable

user experience that can differentiate a product from its competitors.

Chewable tablets, for instance, are a convenient alternative to conventional tablets. In order to survive, human beings learn to chew nutriment from an early age, making chewing a natural process for us. Hence most people find chewable tablets are very easy to take. As they do not need to be taken with liquids, they can be incorporated into daily routines. From a formulation perspective, they are well-suited for converting poorly soluble APIs into a user-friendly form, and various packaging options allow light-sensitive APIs to be stored reliably.

Lozenges that dissolve slowly in the mouth also offer many of the benefits associated with chewable tablets, with the added advantage that they are capable of providing an extended localised effect, in addition to a systemic effect. For this reason, they are ideally suited for treating ailments such as sore throats. The patient experience can be enhanced by adding flavour and a fizzy effect, which can stimulate saliva production and ease dissolution in the mouth.

Orally disintegrating granules (ODGs) are another liquid-free alternative to traditional tablets. They consist of small grains of one or more API that can be poured into the mouth directly from the stick pack (which is a small sachet) and immediately swallowed. As the dosage form is dissolved while swallowing they can offer rapid release of API and excellent bioavailability. With packaging options that include light-protection for photosensitive APIs, and both easy-to-tear and child-resistant packaging, ODGs can be used for a diverse range of products.

Drinkable medicines, prepared by adding effervescent tablets or instant powders ("instant drinks") to water, offer an easy way for consumers and patients to take their medicine, adding benefits associated with increased hydration. As the API is dissolved prior to consumption, they result in excellent bioavailability and rapid absorption, ensuring reliable efficacy. Effervescent drinks form a

buffered solution that increases the pH of the stomach and allows APIs to pass quickly into the small intestine, minimizing gastric irritation.

Both instant drinks and effervescent tablets offer significant potential in terms of flavoring, and are designed to dissolve completely in the glass without leaving residues or foam. As there is almost no size limitation to either dosage form, they allow large amounts of API, or even a combination of APIs to be taken in a single dose.

Taste

A challenge and an opportunity of developing user-friendly dosage forms is that they are tasted more thoroughly than conventional tablets – and palatability of the oral dosage form plays a considerable role in patient compliance. Flavouring and/or taste masking are often required to overcome the typical bitterness or sourness inherent with many APIs.

For user-friendly dosage forms, this opens the door to a wide range of flavouring opportunities for the pharmaceutical industry. Innovative combinations of flavour and application are possible. For example, during the recent development of an orally disintegrating granule painkiller containing caffeine and acetaminophen (paracetamol), HERMES PHARMA chose a cappuccino flavouring in part for its association with caffeine. Careful consideration of the product and its therapeutic application can ensure flavours work in harmony and enhance the user experience.

As taste assessments on new medicine products involve lengthy and costly clinical trials and require approval by an ethics committee, it is therefore important to have a clear strategy based on an understanding of what flavours work well with APIs in order to shorten the formulation development process. Partnering with third-party companies is one way in which pharma can tap into this expertise.

It can be difficult to achieve taste masking using sweeteners and flavourings alone, so other techniques may be used in combination. For ODGs, a coating is applied that prevents API release in the mouth but yet permits release during the window period of the API. At HERMES PHARMA, one method we have found to be

USER-FRIENDLY DOSAGE FORMS

These are designed with the modern patient/consumer in mind helping to improve compliance. They are easy to swallow (even for people with dysphagia) and convenient to take, particularly as they are mostly provided as a single dose. User-friendly dosage forms taste pleasant, can be produced in a variety of flavors and offer consumers choice. Some forms need water in order to prepare a drink (also offering a rehydration benefit), while others can be taken on the go without any liquids.

EFFERVESCENT TABLETS



- Can deliver large amount of APIs
- Low gastric irritation
- Excellent bioavailability

INSTANT DRINKS



- Single dose sachet
- Hot or cold options
- Excellent bioavailability

CHEWABLE TABLETS



- Ideal for poorly soluble APIs
- No need for water
- Convenient - take anywhere, anytime

ORALLY DISINTEGRATING GRANULES



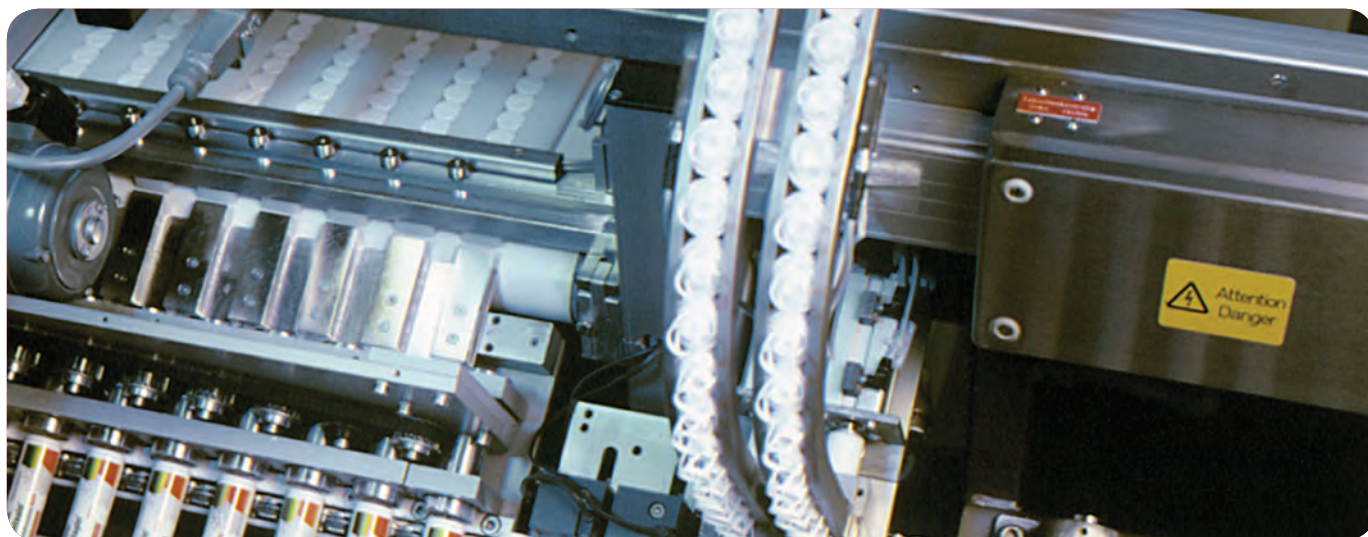
- Pour directly into mouth and swallow
- No need for water
- Convenient - take anywhere, anytime

LOZENGES



- Dissolve slowly for long lasting effect
- Additional localized effect
- No need for water

Figure 1. User-friendly dosage forms at a glance – Overview of some of the benefits of user-friendly dosage forms



particularly successful for ODGs is hot melt coating. Originally developed for the food industry, hot melt coating involves spraying a molten lipid-based mixture onto a solid API particle at carefully controlled temperatures, which then solidifies to form a homogeneous coating. Not only does this method remove the need for organic solvents, but it also provides shorter processing times and lower production costs.

How can Pharma Use User-friendly Dosage Forms to their Advantage?

Rising R&D costs and patent protection issues pose significant challenges to the pharmaceutical industry. Reformulation of existing medicines into new dosage forms can therefore be a particularly useful approach to extending patent protection. Such product lifecycle management strategies make it more difficult for rivals to create similar products, particularly if specialist technologies for taste masking or control of API release are required.

User-friendly dosage forms present not only an opportunity for pharmaceutical companies to extend product lifecycles – they can also build brand equity and increase market share. Alternative oral dosage forms can outperform tablets and capsules when it comes to user experience. In the survey mentioned above, it was clear that people who have had experience with these dosage forms, such as instant drinks and chewable tablets, scored them more favourably than conventional tablets and capsules across all criteria, including taste and ease of preparation. This indicates that they better meet consumer needs, making them more likely to be successful in the market than traditional solid forms. By extending a product range

to meet customer preferences, either through flavour differentiation or by creating more user-friendly formulations, pharmaceutical companies can leverage existing brand equity.

Additionally, innovative pharmaceutical companies can increase their market share and reputation by creating products that are viewed as new and exciting. Alternative dosage forms create opportunities for pharma to develop new products optimised for specialised patient groups, such as children or the elderly, and target new audiences, such as the 'on the go' and sports product market.

Some user-friendly dosage forms, such as effervescent or instant drinks, are less restricted in size than conventional tablets, allowing two or more APIs to be combined in a single dose. This creates opportunities for pharma to develop products that offer multiple health benefits or enhanced efficacy due to co-administration. Single products such as these can remove the need for additional medicines, increasing existing brand loyalty and attracting new users.

With customers demanding convenience, packaging provides another opportunity for pharmaceutical companies to set themselves apart from the competition. User-friendly oral medicines come in a wide range of packaging forms, from easy-to-open sachets to tubes of effervescent tablets. With effervescent tablets, for instance, patented technology such as TOPO granulation can be used to produce stable and humidity-resistant products that still dissolve rapidly when added to water. For products containing light-sensitive APIs, aluminum-coated sachets

can also be used to ensure products maintain their efficacy whilst in storage. Such approaches reduce demands in terms of storage conditions, ensuring products remain user-friendly.

Conclusion

It is clear that while people want convenience and easy-to-swallow medicines and that these improve compliance, many are not happy with the conventional tablets on offer to them. For the pharmaceutical industry, this provides a significant opportunity to differentiate themselves in the market and to revitalise old products by reformulating into new dosage forms and building product ranges.

References

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