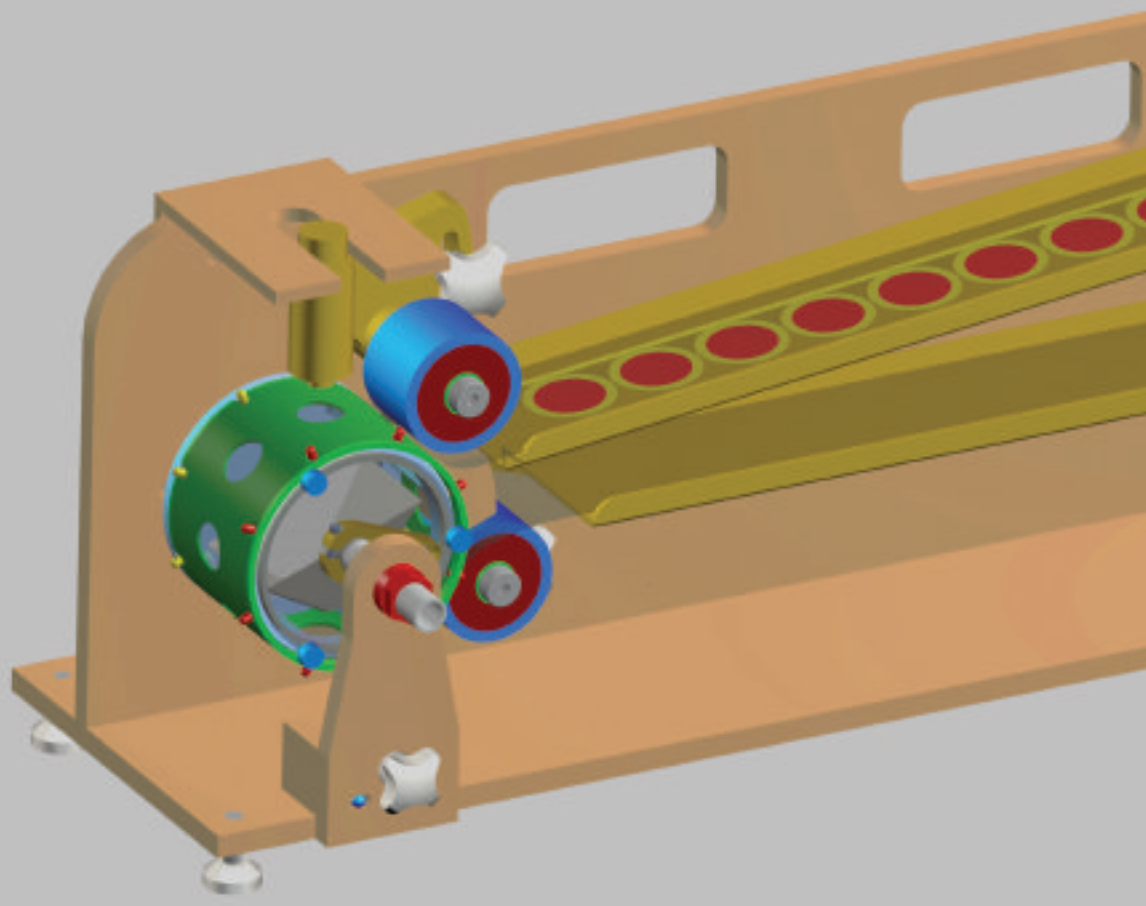

Novel Dispensation

Sticky web technology allows high speed printing of pharmaceutical powders: an innovative method for dispensing APIs that should provide ample benefit to the industry in the long run

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Sticky web is a novel precision powder dispensing technology capable of accurately 'printing' 0.1 to 100mg of powdered active pharmaceutical ingredients (APIs) with a variety of particle size distributions onto edible or inert adhesive webs or surfaces. Accuracies are typically better than around 2.5 per cent and the approach can deliver commercial manufacturing speeds up to 600,000 doses per hour. This article looks at how the technology was first discovered, its promise and its progress towards commercialisation.

Powder handling is technically challenging at the best of times. But accurately filling capsules with milligram quantities of potent APIs at the manufacturing speeds and outputs required for a blockbuster drug adds another layer of complexity entirely. Manufacturers tend to overcome this hurdle by 'bulking out' APIs with excipients for subsequent tablet pressing or capsule filling, but there is also considerable commercial interest in developing high-speed manufacturing technologies to dispense pure active powders. Not least because working with mixtures suffers from one major commercial downside: the need to invest in lengthy and expensive formulation and stability studies – work that adds months, even a year or more to increasingly costly R&D programmes.

Sticky web was first discovered and developed for GlaxoSmithKline (GSK) to target pharmaceutical applications, but has been subsequently shown to be generic and scalable for virtually any market or application requiring high throughput, precision powder dispensing; for example diagnostics, flavourings, fragrances, catalysts and other speciality chemicals.

Dr Keith Smith, manager of GSK's strategic technologies department, says the core technology was the direct result of some "shrewd research": "GSK first appointed the product development

Figure 1 (above): CAD model of a single lane test rig that delivers up to two doses per second. Units can be further optimised and combined in a multi-lane machine to deliver commercial-scale outputs

consultancy to carry out an independent strategic technology review and to evaluate what credible powder-dispensing approaches already existed that could potentially be scaled for high-speed manufacturing. We already knew of some commercial systems claiming speeds up to 15,000 doses per hour, but they typically involve check weighing or volumetric techniques and are often unsuitable for some pure APIs that require careful handling. The consultancy team responded not just with a detailed review of the options but also some new ideas of their own for consideration, including the approach we now call 'sticky web'."

Developing the Technology Platform

Sticky web takes its name from a simple but powerful discovery: when a piece of adhesive tape is dipped into powder and the excess shaken off, the quantity left adhering to it is directly proportional to the surface area of the tape. The exact quantity depends on the combined properties of the specific adhesive and powder, but even those very first tests showed consistent coverage rates of approximately 1.5mg/cm^2, with accuracies better than 10 per cent.

Subsequent development work has helped to develop a stronger technology platform, several adhesives and designs for a production machine, as well as securing a key patent application. The joint development team has also significantly improved the dosing accuracy to approximately 2.5 per cent or better, and with Respitose powders has demonstrated dose repeatability of approximately one per cent.

Powder Dispensing to Deliver Uniform Coverage

Figure 1 (page 50) shows a simplified schematic of the powder dispensing operation at the heart of the production machine. The web, which is pre-printed with adhesive further up the production line, passes around a drum where powder from a vibrating hopper is applied through drum apertures or masks to these sticky areas. A vibrating paddle taps off any excess, which then drops back into the hopper. The technique works well in accurately delivering uniform coverage for powders that are either free running or have dry clumping behaviours, and it is gentle enough for sensitive materials. Some studies have also been undertaken using micronised substrates as a route to lower densities, which would be invaluable for dosing smaller quantities of more potent materials.

The background image opposite shows a single strip of coated film web ready for die cutting into individual doses. Each 2cm diameter area shown here contains approximately 4.7mg of API. The substrate is typically around 50 micron thick which allows the powdered films to be easily rolled or folded for encapsulation or further processing as required. The singulation and packaging processes can be fully automated as part of a complete continuous commercial production line.

Figure 2: Sticky web delivers clean edges for precision powder dispensing

A test rig unit can deliver up to two doses per second. However, further optimisation to improve this rate to 10 doses per second and a multiple lane production machine, for example with 16 lines in parallel, would deliver around 600,000 doses per hour.

Web Films, Adhesives and Dissolution

Aside from the powder dispensing module, the web or film carrier and the printable adhesive are the two other main system components. Edible or inert films such as Monosol F100 are already being used within the food and healthcare sectors; they can be safely ingested while also being robust and flexible enough

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for standard web handling. However, a number of innovative new films are being developed by pharmaceutical and specialist technology companies who are interested in thin-film drug delivery and controlled-release encapsulation, which could potentially be exploited for sticky web.

As part of the initial development, existing edible pressure-sensitive adhesives (PSA) were also examined and a range of new substances developed. These novel adhesives can be printed onto webs, offer instant tack in a dry state and gently adhere to the steel powder dispensing drum, yet peel without leaving any residue. In addition, they offer good powder adhesion and dissolve readily in water.

Figure 2 shows a 20x magnification of a typical powdered area generated with one of these new adhesives. Note the clean edges, even powder distribution and adherence of large and small particles within the sample.

One of the most interesting features of this novel dispensing approach is the potential for improved release of active powders with a tendency to agglomerate during dissolution when they are delivered via powder-coated films versus capsules. Powders delivered via sticky web appear to show greater bioavailability in the bulk system compared with capsules. This could be a real advantage for the technology, although further, more detailed studies and validation would be required for specific adhesive and powder combinations.

Future Developments

The bulk of development activity to date has looked at using edible flat carriers, likely to be the preferred route for pharmaceutical applications, but the adhesive could just as easily be printed onto surfaces, bubbles or tablets that are then subsequently precision dosed with powders. The technology also opens the way for a number of novel and more differentiated dose forms such as: gradient dose printing, for example from 0 to 100 per cent dose in five per cent steps and then perforating the strips; two or more substances combined into the same delivery package; or using controlled release rate films. The approach was initially developed to target pharmaceutical applications, but is applicable to virtually any industry that requires accurate, high production volume dosing of powders to improve existing manufacturing processes or generate innovative new products or processes.

"Sticky web offers considerable promise for high speed production environments where online inspection systems could be used to validate every powdered area and to improve process feedback, increase efficiency and reduce costs," said Smith.

For a technology that started life with a eureka moment involving sticky tape and powder, the commercial possibilities for a number of major markets are virtually unlimited and waiting to be discovered.

About the author

Howard Biddle is Managing Director of 42 Technology (42T) – a product design and development consultancy, based in St Ives near Cambridge. He started his technology consulting career as a junior engineer at Cambridge Consultants and rose through the ranks to become CEO, and joined 42T in 2002. Howard has been named in many patents including the Bass 'widget', several drug-delivery devices, a novel tablet manufacturing system and a new aerosol technology. He has a degree in Mechanical Engineering from Queen Mary College, London and a Master's in Industrial Design from the Royal College of Art.
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