



Laminated, folded, encapsulated

So much for capsules can only be filled with powders, pellets, micro-tablets or liquids! The Accordion Pill® by Intec Pharma Ltd. is a drug delivery system that uses active ingredient containing polymeric films, which are folded into an undulated shape. This system combines an efficient gastric retention and specific release mechanism. The manufacturing technology for this innovative product was developed in close cooperation with Harro Höfliger.

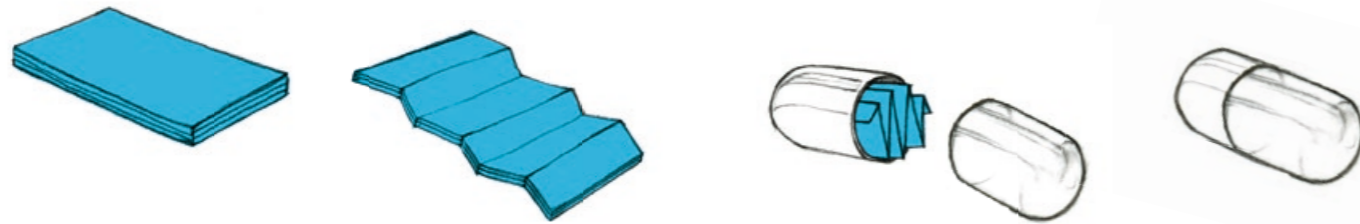
It is a problem that affects millions of patients around the world: After the intake of drugs, the level of active substances rises in the blood, reaches a peak and then subsides. To ensure that the level of active ingredient in the body is always within the appropriate concentration range, it is necessary to take the medication at regular intervals. For many patients, however, this poses an enormous challenge in coping with their daily routines, and reduces their quality of life. Due to the fluctuation range, the optimal level of

active substances is often available for a limited period only.

The Israeli enterprise Intec Pharma has addressed these issues by developing the Accordion Pill® platform. The Accordion Pill® looks like a normal capsule, however, its interior contains a small folded GRDF, short for “Gastro Retentive Dosage Form”, which consists of several layers of biodegradable polymeric films and the active substance. The Accordion Pill® is named after the characteristic folding of the GRDF, which is reminiscent of the musical instrument.

The Accordion Pill®

The Accordion Pill® is a unique delivery platform based on folded multilayer films. It provides a better treatment by improving the pharmacokinetics of drugs with narrow absorption windows or poor solubility. Furthermore, it allows fixed-dose combinations. Safety and efficacy have been tested in more than 30 clinical studies, with tens of thousands of administrations.



“It was a long way to today’s completely automated production.”



Ronny Reinberg,
Vice President Technology Affairs
at Intec Pharma

substances lasting usually for only two to three hours when taken orally.

The Accordion’s production is as complex as the innovative nature of this dosage form. “Depending on the type of application, different web materials must be laminated and welded, followed by punching and folding of the GRDF before it is encapsulated,” explains Ronny Reinberg, Vice President of Technology Affairs at Intec Pharma.

From manual stations to a state-of-the-art line

Development was equally complex. “In the initial stage, we manufactured the Accordion Pill® in a completely manual process by using a self-designed folding unit, among other things. It was a long way to today’s completely automated production,” says Ronny Reinberg.

In 2013, when Harro Höfliger was commissioned with the development of a pilot-scale system for the production of clinical supplies of the Accordion Pill®, the company could draw on the experience gained with the manual stations. “When it comes to complex products and special solutions such as the Accordion Pill®, it always makes sense to start with smaller machines in order to acquire production experience,” explains

After taking an Accordion Pill®, the capsule dissolves in the stomach, the GRDF unfolds and releases the active ingredient continuously over a period of eight to twelve hours. This also applies to

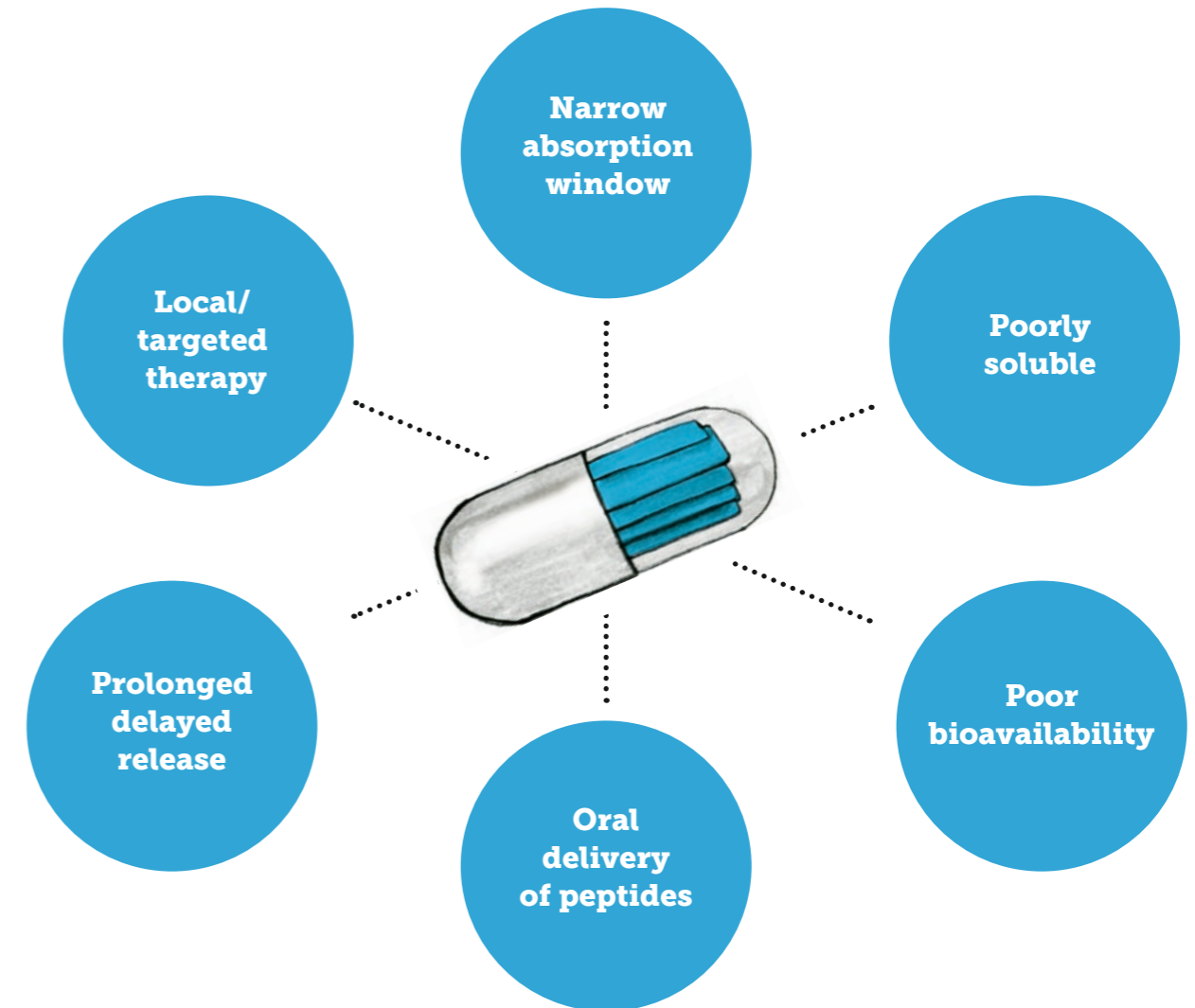
About Intec Pharma Ltd.

Intec Pharma Ltd. is a biopharmaceutical company focused on developing drugs in the clinical stage on the basis of its proprietary Accordion Pill® platform technology.



Intec Pharma Ltd.

A solution to challenging pharmacokinetics



Frank Erbach, Senior Sales Director at Harro Höfliger. “This is why we designed a PML version – our small web processing machine – which was precisely tailored to the expertise gained with the manual machines.”

In 2017, this was followed by the order for a high-performance line. While the web material on the pilot-scale line was still processed in intermittent mode and on two lanes, the high-performance line is operated in continuous motion on ten tracks and achieves an output of up to 360 products per minute.

The centerpiece of the line is the PMK, a production platform for web processing. As with the PML machine, the

various GRDF layers are first joined together. Folding stations then fold the GRDFs into a compact format before encapsulation with a Modu-C machine. The line is completed with the Accura-C, a capsule weighing system for quality assurance.

Ronny Reinberg is very satisfied with the cooperation: “Our Accordion Pill® is by no means an ordinary product. For this reason, Harro Höfliger carried out tests, for example extensive proof-of-principle of the critical stations. Thus, we have jointly succeeded in making the leap from manual machines to pilot-scale equipment to high-performance production.” ■