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Pigs, pineapples and a prison fire: MediWound founder's long road to approval of anti-burn ointment

At a secret location in Asia there is a vast pineapple field intended for the production of an ointment to heal burns • This product, developed by MediWound, was recently awarded FDA approval, breaking a long dry spell for Israeli companies • The founder of the company, Prof. Lior Rosenberg, tells about the strange meeting with the scientist who started it all and about the new experiments in treating wounds and skin tumors

By: Gali Weinreb

At a secret location somewhere in Asia, there is a vast pineapple field. Miles and miles of pineapples. Every 30 tons of pineapple stem eventually become one kilogram of medication for burns and wounds in the hands of the Israeli company MediWound.

This medication made headlines this week after it was awarded FDA approval for marketing in the USA, breaking a dry spell in approvals that had lasted for decades. Other than Teva, no Israeli company has received FDA approval to market a preparation with a new mechanism of action.

Now doctors have to be persuaded to put down the surgeon's scalpel, or rather the surgeon's peeler with which they remove layer after layer of burned skin, and instead remove the skin using pineapple extract. The company's experience in Europe shows that this is not always easy, since the surgeons have become used to their cutting tools, but it is possible.

The idea of an outsider scientist in the USA

The story of this medication actually does not begin in the pineapple field, but in a POW camp in Africa during World War II. German prisoner of war Dr. Gerhard Klein and an American nurse who treated him fell in love, and following in the footsteps of this love, Klein came to the US.

"He was looking for work and came to surgeon Dr. John Berk, who didn't really want to hire him as a doctor because he didn't trust German medical training," says Prof. Lior Rosenberg, the founder and medical director of MediWound. "But Berk also headed a group of researchers who were trying to find an enzyme that would remove dead tissue from burn wounds, so he sent Klein to search for it."

Rosenberg went on to say that Klein used his research budget to buy pigs. "He would give them burns, try to treat them, and end up eating them," he said. Eventually he found the enzyme that is able to break down the dead tissue only. "We really don't know why the pineapple stem developed these properties."

Klein, says Rosenberg, "was a suspicious man even back in Europe, and he thought that everyone wanted to steal his invention. The cultural differences between him and the

Americans were pronounced, and he was unable to get them interested in the product. Finally in 1982, he went to a conference in Switzerland."

Rosenberg, who was a surgeon at Soroka Hospital at the time, also attended. "Klein presented a picture of a pig, and then how he applied the miracle salve to it, and look – there's a result. But he was so afraid of confidentiality that he moved the pictures on quickly, and it was impossible to see anything. The audience began to get bored and chatter, and suddenly he pulled down his pants and showed us his bare leg, on which a blue square was drawn.

"He said: 'I have anesthetized this area,' and then he took out an iron. He placed the iron on his leg. It completely burned the skin! Then he said, come to room so and so at the conference hotel at 4:00 p.m., and see how the place has healed."

Rosenberg was already there at 3:30 p.m., and was sure that the corridor would be filled with curious people, but he was all alone. "Apparently such crazy things are not for the Americans or the Swiss, but they are for Israelis. Klein unwrapped the bandage, and I saw something strange. I didn't know if it was clean or not, but I was intrigued."

At that time, the world was no longer looking for an enzyme for debridement, and the peeling method had been developed, in which the skin is removed layer by layer. This method is effective, but creates a lot of bleeding, and requires the removal of healthy tissue around the burn tissue, and also the use of a skin graft taken from an area of the body with healthy skin. "I hated that surgery," admits Rosenberg. "It's a life-saving method, but comes with complications and scars."

Identity card
MediWound

Field of activity: Healing wounds and burns using an extract produced from the pineapple stem. The current CEO of the company is Ofer Gonen.

History: Established in 2000 by Clal Biotechnology Industries together with Prof. Lior Rosenberg. Received private investments of some \$40 million from Clal Biotechnology Industries, Gandyr, Harel and Migdal. In 2014, it was listed on Nasdaq. Since then, the stock has lost 91% of its value, but the company was able to raise about \$150 million in this way. Today it is traded at a value of \$73 million.

One more thing: Received EMA approval in Europe in 2012, and FDA approval in December 2022

Growing a pineapple for a cookie

Rosenberg received exceptional approval from the Israeli Ministry of Health to conduct a clinical trial for a product that had not been trialed by a regulated company, and without the trial having received approval elsewhere in the world. "The success rate was about 50%," says Rosenberg. "I continued to try it on pigs that I bought from Kibbutz Lahav. I treated several hundred pigs and around 80 people until the 1990s, and then the material that Klein had given me ran out.

"In the interim, Klein had died, but I continued to develop the method. I discovered that the product could not be used together with silver or iodine, and other changes that were important for the product's activity. I taught myself how to produce the substance in a more reproducible way than Klein's method. I also designed a unique dressing in which the gel

remains for four hours." Today the preparation works in almost 100% of the cases, and it turns out that for the most part it is possible to avoid the use of an autograft and damage to another area of the body.

In 2000, he received a call from David Hazelkorn, former CEO of BTG, who had retired and founded Clal Biotechnology Industries to invest in companies engaged in the life sciences. "Is the pineapple still available?," he asked. And that's how we founded MediWound."

But life was not easy.

"We went through ups and downs. Anything you can even imagine happened to us. It took us a while to make contact with a pineapple grower who would grow the exact pineapple we need. It's not a good pineapple for eating, so in order for it to be worthwhile for the grower, we had to invent a type of cookie to make from it, so that the raw material would not go to waste."



MediWound's pineapple field in Asia / Photo: MediWound

It is rare for the FDA and the European Authority EMA to approve a medication whose source is a plant extract. Such products are usually routed to the world of food supplements.

"Many drugs were produced, at least in the beginning, from plant extracts, for example aspirin and quinine. Our product is a medicinal product, because we know how it works, because we can produce it so that it contains exactly the same quantity of active ingredients each time, and because we have proved its effectiveness in a clinical trial at the level required for a medication.

"Dr. Eilon Asculai, head of our R&D, sat down and organized all this information and submitted it to the authorities, who accepted the extract as an indisputable medication. We had some nice surprises along the way too, and this was one of them."

Even before you received the approval, you had an agreement with Teva, which was canceled.

"This was a short story, in which they financed our development and purchased an option to market the product, but then there was a change of management, and Dr. Jeremy Levin, the incoming CEO, decided to focus on oncology and neurology. He returned the product to us.

"When this agreement ended, we didn't know what to do, but at that time we didn't know what to do every two weeks, and every minute it seemed like the money was running out anyway. What could we do? We kept swimming, like the frog in the milk, until we became butter."

The conservative nature of surgeons in Europe

In 2012 you received approval in Europe, but it took a while for revenues to follow.

"Suddenly someone comes along from a Levantine country and says, 'This ointment does your job better than you.' In some cases, this was very insulting. In Germany they were conservative. In England they said, 'Look, we invented surgery in the time of Queen Victoria, are you going to teach us to operate?' I said, 'I'll teach you how not to operate.' And a lovely surgeon wrote an article called 'Let's put down the knife.'

"There was also anti-Semitism. We received a letter from the director of a burn department saying that the product is tempting, but they won't use it because it comes from Israel. The Italians who were the most open to us. What's funny is that the directors of the burn centers in Italy were all people with huge egos, who could not be brought together without an explosion. They joined forces to write the protocol promoting the use of our product, and today they go to the beach together."



Prof. Lior Rosenberg / Photograph: Eyal Yizhar

Identity card

Prof. Lior Rosenberg

Personal: 77 years old, with three daughters and eight grandchildren

Professional: Professor Emeritus of Plastic Surgery, founder of MediWound, and currently serving as medical director of the company

One more thing: Founded the Museum of Medicine at Ben Gurion University and the Carasso Science Park in Beer Sheba. Initiated and led surgical delegations to Africa and Asia. Received a knighthood from the Order of the Knights of Malta.

In the third quarter of 2022, the company recorded revenues of \$1.4 million from the sale of its products alone, but this is an activity that has so far been limited by the company's available cash and managerial attention. In the USA, the product will be marketed by a partner called Vericel, which operates in the burn sector and already has a distribution network in the country. At the same time, MediWound has received approval to market its product to the pediatric burn market in Europe, which is larger than the adult market, it has increased the number of approvals in specific European countries, and it has received approvals in several other countries around the world.

Champagne and dancing on the table

A year and a half ago, the product was about to be approved, but the approval was postponed. "I think they were busy with Covid, and in fact they begged us to delay submission of the application ourselves, so as not to be a burden on their pipeline," says Rosenberg. "They did this by way of submitting questions for correction, and we were perhaps arrogant and said 'no, no, we can answer everything,' and then, instead of postponing submission ourselves for six months, they postponed it for more than a year.

"The official explanation was that some of the doctors knew which group the patient was in. What really happened is that some of the doctors simply couldn't be bothered to sign the form saying that they did not know which patient had received which treatment. We simply did not take enough care to get this signature from the busy doctors, but we showed that even if these doctors were aware of the division into groups, our results were still very good, and then the product was approved, with minor corrections."

This approval even came a few days before the last possible deadline set by the FDA.

"Suddenly I heard Ety Klinger, our Chief R&D Officer, let out such a shout that I thought she was giving birth or something. We celebrated with some bottles of champagne we had in the office. One of the managers had said that if we got approval he would dance naked on the table. And he danced. But not naked".

The agreement that saved the company

Rosenberg says he owes the company's success to an agreement signed in 2012 with BARDA, the American Biomedical Advanced Research and Development Authority for emergency protection in the biological sphere. Shortly before, Rosenberg was simultaneously treating eight victims of a prison fire, and he realized that in an emergency, the company's product had a great advantage when treating multiple patients at once,

because not only surgeons can apply the ointment. Burn wards are small, and a large fire can fill them fast. According to Rosenberg, since then it has been his mission to promote the product as an emergency product.

"Fortunately, my life is intertwined with all kinds of amazing people," says Rosenberg. "All kinds of leeches as well, but also amazing people, and Narayan Iyer, who was then head of burn countermeasures at BARDA, is one of them." Initially the meetings were secret, until he decided to promote a joint development contract between the parties.

BARDA financed the company to the tune of approximately \$200 million, and in return was equipped with emergency medication. No less important than the money, this gave the company credibility in the US, and also in the American capital market, where it began trading in 2014. "It saved the company," says Rosenberg.

Today MediWound is preparing for the start of marketing in the US, for continued marketing in Europe, and for the continuation of clinical trials for additional indications. The company is engaged in advanced trials in the field of chronic wounds, and recently began trials for the treatment of skin lesions, after Rosenberg successfully treated his daughter. "And we have more applications up our sleeves," he promises.

"Will the product remain in Israel? In MediWound's hands? I don't know, but it already exists and has passed the point of no return."