Bayer Buys Rights to Market GWP's Cannabis Extract

By Fred Gardner

GW Pharmaceuticals, the British company that has conducted successful clinical trials of cannabis-based medicines, has signed a deal allowing Bayer AG to market one of its tinctures in the UK under the Sativex(r) brand. Bayer also gets a limited-time option to negotiate marketing rights in Europe and "selected other countries."

GW gets a cash infusion from Bayer to push forward with research, production, and clinical trials —plus a cut of future sales proceeds. Its stock on the London Exchange has risen from about 190 to about 250 in recent weeks. GW stock rose sharply earlier this spring when the company applied to the Medicines and Healthcare Products Regulatory Agency (the British equivalent of the USFDA)

DAVID WATSON AND GEOFFREY GUY IN 1998

for approval of Sativex as a treatment for severe neuropathic pain and multiple-sclerosis symptoms. Bayer is betting that in the months to come, the MHRA will approve Sativex or kick the application dossier back to GW with requirements that can be fulfilled readily.

GW was launched in 1998 by Geoffrey Guy, MD, a pharmaceutical entrepreneur whose first canny move was to buy all the seed strains collected and refined over the years by Hortapharm AG, a Dutch firm run by two California expatriates, Dave Watson and Robert Clarke.

GW's drug-development strategy was based on the assumption that various

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components of the cannabis plant beneficially modulate the effects of THC and exert helpful effects of their own. Guy inferred from the literature that the cannabis Queen Victoria smoked to alleviate menstrual cramps was rich in cannabidiol (CBD), and he hypothesized that CBD, not THC, was the key anti-convulsant component. To date GW has bred plant strains in which six different "cannabinoids of interest" predominate. The only ones to have been used in clinical trials are high-THC (which GW has dubbed "Tetranabinex"), high-CBD ("Nabidiolex"), and a 50-50 mix ("Sativex").

In addition to at least 66 known cannabinoids (21-carbon atoms in ring structures, with hydrogen and oxygen molecules attached at different points), the cannabis plant contains hundreds of compounds that are not unique to it -terpenes, flavonoids, amino acids, fatty acids, proteins, sugars, hydrocarbons, simple esters, steroids, nitrogenous compounds, vitamins, elements, and more. Terpenes produced in the glandular trichomes are the essential oils that give cannabis its smell. GW researchers hypothesize that certain terpenes may have anti-ulcer and anti-mutagenic potential. So GW's approach has been to grow plants with desired cannabinoid ratios and blend them —"trace"components and all— into treacley extracts that can be administered in defined doses by spraying into the mouth. To date the extracts have been used in randomized double-blind trials involving patients with multiple sclerosis or neuropathic pain at four UK hospitals. Significant reductions in pain and spasticity have been reported. According to GW's May 21 press release, "GW is to be responsible for commercial product supply and has entered into a supply agreement with Bayer. GW will manage the supply of product through a range of contract manufacturing partners, arrangements for which are all in place."

Aspirin: Bayer's First Blockbuster

Bayer's original blockbuster drug, aspirin, is also plant-derived. The active ingredient, as patented by Bayer in Germany in 1899, is acetylsalicylic acid.

"The name itself," wrote H.O.J. Collier in the November 1963 *Scientific American*, "represents one of the first exercises in the peculiar art of applied etymology that the merchandising specialists of the pharmaceutical industry have brought to such a high point of elaboration today. The prefix 'a-' stands for the acetyl group… The root, 'spir,' stands for *spirsaure* (salicylic acid) distilled from the flowers of the meadowsweet (*Spiraea ulmaria*)."

Salicylic acid was also derived from willow bark and oil of wintergreen. The first paper to describe medicinal effects from any of these sources was read to the Royal Society of London in 1763: "An Account of the Success of the Bark of the willow in the Cure of Agues," by either Edmund or Edward Stone (a printer's error in the Philosophical Transactions leaves the credit up for grabs forever).

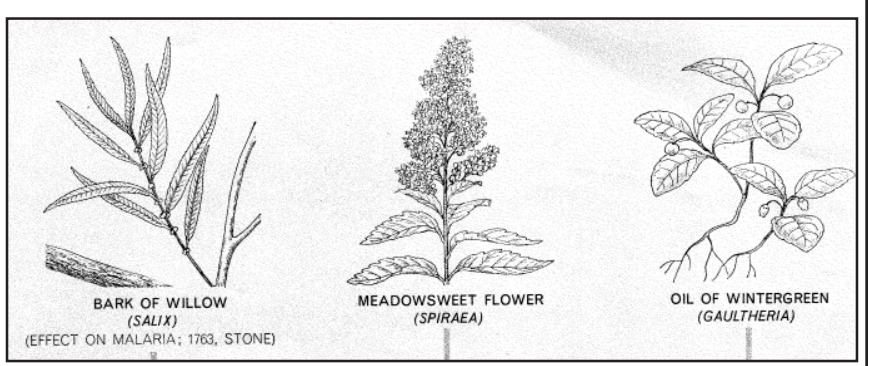
A century later the fever-reducing and anti-inflammatory effects of salicylic acid were well known but "its success was diminished by the irritation and damage it caused to the moist membranes lining the mouth, gullet and stomach." It was not until the late 1890s that Bayer chemist Felix Hofmann found a simple way to make salicylic acid in a less irritating form by adding an acetyl group.

Aspirin is not benign, however, and to this day, worldwide, it causes thousands of deaths annually due to allergic reactions and gastrointestinal bleeding. Advocates of legalizing cannabis for medical use often remark the irony of aspirin, with its occasionally fatal side effects, being sold over the counter while their benign herb of choice remains prohibited.

(Rosie, who is rarely wrong, notes that the dangers of aspirin have been over-publicized by the makers of Tylenol.)

One of the FDA's present requirements is that a manufacturer seeking approval for a new drug explain its mechanism of action. The steps by which aspirin reduces pain and fever are not precisely known. "It has always been easier to catalogue the wide application of aspirin to man's commonest ills than to explain its mode of action," wrote Collier. "There is no doubt about the usefulness of the drug. If the precise nature of its biochemical action remains a mystery, it is because so little is known about the biochemistry of the defensive responses, such as pain, fever and inflammation, evoked in the body by disease."

The same could be said of Sativex in 2003.



THREE PLANT SOURCES OF SALICYLIC ACID.