

SECRET

Visit to Stowic Resources Ltd., Stow-on-the-Wold, Glos.
February 4th, 1992.

Stowic Resources Ltd is a small family business, which manages the production and sale of a range of beauty products. Mr Tucker also works as a financial consultant.

In collaboration with workers at Leicester polytechnic, Stowic have developed and patented a transdermal drug delivery patch which uses novel technology. Despite the current launching of other nicotine patches by a least 5 major pharmaceutical companies, Stowic believe their product will be a serious competitor due to the following claimed advantages;

1. The Stowic patch utilises the hydrophilic nature of nicotine to give a continuous (zero order) nicotine output which is independent of the concentration of nicotine in the patch. High dose patches can therefore be produced without dramatically increasing the patch size. Other patches work by simple diffusion. With these patches, the initial release of nicotine is faster than the rate at which nicotine can pass through the skin. This leads to a build up of nicotine in the skin, causing irritation. More importantly, due to interindividual variation in skin absorbency, the rate of transfer to the blood varies greatly between subjects and can lead to high, potentially toxic doses in some subjects. This is apparently avoided by the Stowic patch.
2. In patient trials, plasma nicotine levels rose earlier (after 1-2 hours), reached a higher peak level (18-20ng/ml) and plateaued at that level for longer (7 hours), when compared with the profiles produced by some other patches. Dr M Russell, Maudsley Hospital, is the undoubted expert on nicotine patches, having conducted patient trials on most of the patches being developed, including the Stowic patch. He is reported to agree that the Stowic patch has high potential but, in a personal communication, has warned that the trials conducted so far are only preliminary and were performed using a prototype patch.
3. The Stowic patch is worn for only 16 hours rather than 24 hour, therefore avoiding symptoms of nicotine delivery during sleep (sweating and vivid dreams).
4. The patch will appeal to the consumer in that it is smaller (10 cm² for a 30 mg nicotine patch), easier to apply and has better adhesion.
5. Unlike with some of the competitors' patches, there have been no problems with leakage of the nicotine gel or skin irritation.
6. It is simple to produce, using blister packaging techniques, needing less equipment and space than production of competing patches. It will therefore have a lower sale price.

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7. The technology of the patch design would apparently need very little adaptation in order to deliver other hydrophilic drugs. Patches are currently being used by pharmaceutical companies for hormone replacement therapy and the delivery of analgesics and other drugs.

Transdermal delivery is, at present, the most effective substitute method of delivering nicotine. Nicotine absorbed from gum is mostly metabolised in the liver before it reaches the brain. Nicotine nasal sprays come closest to mimicking the rapid nicotine absorption from a cigarette, but have experienced problems in clinical trials and are thought to have been withdrawn from development. The patch is also advantageous in that, unlike with gum, there is no reinforcing activity associated with the nicotine delivery, making it unlikely that people will claim to be addicted to the patches.

There are three areas in which the nicotine patch may be used;

- i) smoking cessation - efficacy trials have been inconclusive although a few studies have shown a small increase in successful abstainers among users.
- ii) therapeutics - relief of symptoms and possibly prevention of mouth ulcers, ulcerative colitis, Alzheimer's disease and Parkinson's disease.
- iii) smoking replacement - such products could be used by smokers in environments where smoking is restricted. Some users have also been pleasantly surprised by the enhancement of their powers of concentration.

Once in an established market, the patch, rather than smoking, will be associated with the beneficial effects of nicotine. It may therefore be advisable for BAT to demonstrate support for the development of nicotine as a therapeutic agent.

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