Everything You Need to Know About Recommending or Working with Curaderm-BEC5.

Product Information Guide Booklet

Why become our Partner or Associate?

The world is currently facing epidemic rates of skin cancer. In some demographics the occurrence rate is as high as 50%. Basal Cell carcinoma and Squamous Cell carcinoma, also known as non-melanoma skin cancers are the two most common types of skin cancers. Sun spots and Keratosis Tens of thousands of cities are in areas that are at high risks of developing these skin cancers in their populations. Practical medical help is needed urgently to treat these potentially deadly and devastating afflictions.

info@curaderm.net
Head Office: +678 50986, +678 25898, +678 50987
Customer Contact Centre: +1 602 490 8030
www.curaderm.net
1. Introduction to Curaderm-BEC5

1.1 Epidemic Rates of Skin Cancer

The world is currently facing epidemic rates of skin cancer. In some demographics the occurrence rate is as high as 50%. Basal Cell carcinoma and Squamous Cell carcinoma, also known as non-melanoma skin cancers are the two most common types of skin cancers. Tens of thousands of cities are in areas that are at high risks of developing these skin cancers in their populations. Practical medical help is needed urgently to treat these potentially deadly and devastating afflictions.

1.2 Curaderm-BEC5 the Treatment of Choice Customers are Waiting For!

The established treatments for non-melanoma skin cancers are surgery, Mohs technique, cryotherapy, curettage with cautery and radio therapy. However, in recent years, Skin Cancer Clinics, Medical Professionals, Magazines, Naturopaths and Consumers throughout the USA, United Kingdom and Australia, have increasingly been recommending Curaderm-BEC5 as the Treatment of Choice for non-melanoma skin cancer. In fact, over 100,000 people have now used Curaderm-BEC5.

You may not be aware that this cancer research has existed for over twenty years in Australia. The research has resulted in identifying Solasodine Glycosides which are glycoalkaloids, and are extracted from plant material, with excellent antineoplastic (anti-cancer) activity using a novel mode of action.

This work has resulted in interest world-wide and many centres are elaborating on the Australian findings.

Phase II clinical trials for internal terminal tumours using the glycoalkaloids are now underway in Western Australia. We will have to await these results to see how effective these new antineoplastics are for internal cancers in man.

However, we do not have to wait for a simple, novel, elegant Skin Cancer Treatment, as Curaderm-BEC5 Cream is the only clinically proven treatment now available. This product has over 2 decades clinical experience for the treatment of BCCs, SCCs and Sunspots.

The original research carried out by Dr Cham in Australia has now been confirmed by a plethora of scientists world-wide. In particular the effective treatment of BCC with Curaderm-BEC5 has now been confirmed by ten independent centres in the United Kingdom. These centres have completed Phase III and open studies using Curaderm-BEC5 for the treatment of BCCs and the dermatologists at The Royal London Hospital concluded that with Curaderm-BEC5
"We consider that this rate of treatment success more than justifies the physician considering alternative to currently predominant treatments such as surgical excision or cryotherapy. In our view and experience [Curaderm] BEC5 is a topical preparation, which is safe and effective, ideal therapy for outpatient treatment.

Hence [Curaderm] BEC5 is a much needed alternative to surgery for basal cell carcinoma. This is the commonest cancer in Caucasions worldwide and the prevalence continues to increase with an increasing ageing population. It is a cost effective treatment for both primary and secondary skin cancer care."

1.3 Your Company’s potential participation and benefits with this remarkable product

During 2005, Curaderm-BEC5 was made available to consumers world-wide for home delivery personal usage. The now established “internet skin cancer treatment and help centre” has a captive market of internet users searching and purchasing for home based treatment. However, there is a clear and present opportunity for reputable sellers or health professionals of therapeutic products to incorporate Curaderm-BEC5 into their product portfolio and achieve significant market share and financial rewards for investment in awareness and sales of the breakthrough medicine.

2. About Us and the Legacy of Curaderm-BEC5

2.1 Mission Statement

The company’s goal is to ensure the world gratifies Dr. Cham’s breakthrough research and the product is given its rightful place in the medicine cabinet.

Our aim is to be a global player and establish ourselves as a trusted manufacturer of breakthrough skin care products and export them in key markets of the world.

2.2 The Company’s Objectives are:

- To Make Curaderm-BEC5 available to the world every day of the year, 24 hours a day easily and quickly so that the alarming number of people suffering from Skin Cancer can be treated without unnecessary surgery or toxic drugs.
- To operate with world standard manufacturing, customer service, technology and always professional and ethical standards.
- To educate the Doctors and Dermatologists of the world that there is an alternative available that can treat skin cancer without surgery.
- To continually build the awareness of what is curaderm-BEC5 to people everywhere whether they are in the market to buy the product or not.
- To provide up to date information and help on skin cancer so that people may be more enlightened to the risks of UV exposure.
- To provide rewarding careers for the company’s employees assuring a variety of professional and social experiences.
• To be a valuable member of local Vanuatu economy and contribute wisely to the nation of Vanuatu’s development. Vanuatu is in Australiasia – North East of Australia, close to Fiji.
• To expand the product range to manufacture and market a variety of equally needed products.
• To return profits to the shareholders, wholesalers and technology holders.

2.3 Curaderm Brand History

The brand Curaderm was originally manufactured and distributed by Cura Nominees Pty Ltd in Australia. This followed full clinical trials and monitoring of participants beyond five years. The brand was immediately popular as an over the counter medicine in Australia. Over 60,000 units of Curaderm were sold in the first few weeks of release of the product.

The rapid popularization of the effective treatment lead to a lobby movement by the Australian Dermatologists and Skin cancer surgeons. The lobbying efforts lead to Curaderm to becoming re-classified to prescription only status. This action severely affected the brands reach, however, sales and excellent treatment results continued throughout the 1990’s. Cura’s restricted Curaderm sales were balanced by the company manufacturing other successful cosmetic and therapeutic products for the Australian market.

Dr. Cham was disappointed with the Australian medical system reclassifying Curaderm so that information on Curaderm was hidden from the consumer. By 2000, a Double Blind Randomised Vehicle controlled clinical trial with leading United Kingdom Dermatologists and Hospitals was arranged. A primary objective of this trial was to prove the treatment to be a safe home based treatment. The excellent results paralleled results from clinical trials in Queensland during the 1980’s and completely refuted all wrongful statements suggested by the Australian Dermatology lobby.

Despite this irrefutable evidence, Curaderm was not given any praise by the Australian dermatologists about the United Kingdom clinical results. Even the Australian Medical Journal was not cooperative to publish the excellent results so the Australian doctors could be more informed and prescribe the treatment to consumers.

With Curaderm in such a restrictive position within the Australian market it was decided the entire brand including manufacturing, management and distribution would be moved out of Australia. Since 2004 Curaderm Global Limited has been established in the Australasian Pacific Islands of Vanuatu with a new vision of creating a global brand

Curaderm.net was launched during 2005 to promote the clinical value of Curaderm as an effective home based skin cancer treatment. The brand name was extended to Curaderm-BEC5 to incorporate the success of the 2002 United Kingdom clinical trials which used the registered the trial under the clinical name “BEC5”. Millions of people beyond Australia have subsequently been enlightened to the availability of Curaderm through online web search, news releases, blogs and medical websites.
The internet has promoted the strong medical science and clinical results, taking the brand beyond the internet to a series of health journals, newsletters, TV footage, magazines and specialized Doctor Networks. Distribution and Approvals for the medicine to be sold at retail pharmacies and health stores are now underway in a variety of countries including USA, South America, Caribbean, Middle East and New Zealand.

2.4 Board of Directors

Chairman
Tania Chase
Director@curaderm.net

Tania Chase is an experienced business manager and investor and headed the branding and distribution of Curaderm in the Australian market. The company Cura Pty Ltd manufactured a variety of cosmetic products offering excellent therapeutic value to a strong and loyal Australian customer base. Tania brings to the company a wide range of experience in manufacturing and distribution of health products and has been personally involved with several large USA and Australian medical companies.

As Chairman, Tania is responsible for overall Corporate vision and Heads Manufacturing. Tania has had decades of experience with Curaderm and provides excellent knowledge into treatment and product information.

Chief Executive Officer
Simon Agius
B. Comm (Mark, Acct)
Wholesale@curaderm.net

Simon entered the Natural health sector in 1996 establishing a medical herbs import company in Australia. He managed a variety of herbal processing businesses operating in Australasia and distributing the products in the USA, Japan and Europe. By 2000 he launched a new cosmetic oil in the USA market, True Tamanu Oil, now popular with USA health stores and cosmetic formulators. Between 2002 and 2004, Simon worked in the United Kingdom Natural health wholesaling and health websites. Simon is an excellent communicator and team player.

As C.E.O, Simon heads Branding and Distribution and works closely with the Board and Sales and Management team to execute business plans that achieve maximum exposure and excellent brand reputation to a loyal and growing customer base.

Scientific Advisory Board
Dr. Bill Elliot Cham

Dr. Bill Cham, PHD, is the Head of the Scientific Advisory Board. Dr. Cham’s published research references and other related information is included within this introduction.
Dr. Cham is now retired in the Pacific Island country of Vanuatu however, he regularly participates in media interviews and other publicity. Dr. Cham is available for appropriate Medical Conferences or Publicity invitations as the inventor of Curaderm-BEC5.

Sales and Marketing and IT Executives

Our dynamic Business Unit Managers have decades of experience with sales and marketing organisations in health, web, fitness industries and other sectors in both North America, Europe and Australasia. It is our absolute priority for your business to take advantage of our Curaderm-BEC5 sales and marketing experts so that you can achieve a very quick revenue stream from your current customers, database and ongoing visitors.

Stan Phani  
Head of Sales, Publicity  
Sales@curaderm.net

Tem Zerighaber  
Head of Marketing and Affiliate Management  
Marketing@curaderm.net

Jean Paul Stivala  
Head of Web Branding, IT and Design  
IT@curaderm.net

Curaderm-BEC5 Business Unit Managers mentioned above are available to personally assist with your strategy to achieve regular cash flow for your organization. The will also outline our excellent Product Support Specialists, whom are also available for you and your customers.

2.5 Head Office and Contact Centres

Head Office

In 2004, the Head office for Curaderm-BEC5 manufacturing and distribution was moved to Vanuatu, South West Pacific. This move reflected the change of focus for the brand away from Australia and toward the entire world market. Vanuatu also provided Dr. Cham and his family a healthy lifestyle in the beautiful pacific islands. All management and head office operations have been situated in the capital, Port Vila, known as the Pacific Islands Finance centre. The National Government supports the companies vision to eliminate skin cancer world wide. Vanuatu is serviced by world class Banks, Accountants, Logistics firms and E-Commerce capacity.

Call Centres
Our call centres are now operating in the Pacific and Europe under business services utilising the Curaderm-BEC5 customer information global information network.

**Phoenix Customer Drop Zone Contact Centre**

We have recently established a drop zone in Phoenix for US Post contact and mail drops. This means companies can now send cheques and orders easily.

**2.6 Curaderm.net Website Retail & Wholesale Operation**

Curaderm.net has been growing sales and awareness throughout internet users searching for information on skin cancer and treatment options. The vision is to make Curaderm-BEC5 as common as any home brand. The diagram below shows real visitors tracked on the google network during recent months. You can see the expansive territory already covered through online marketing of Curaderm.net.

The company’s distribution plan is to maintain awareness strategies and provide mutual financial benefit for organisations that can further distribute and/or create awareness of Curaderm-BEC5 through wholesale, retail, direct, news or internet placement. Over the past year, more and more doctors, naturopath’s, health stores and websites have been purchasing Curaderm-BEC5 for customers.

The company has now invested in new technologies for proper wholesaling direct to Retail and Medical Professionals worldwide.

**2.7 Manufacturing Operations**

Curaderm-BEC5 is manufactured at a pharmaceutical company in Auckland, New Zealand. The facility is managed by strict quality control to ensure the manufacturing of superlative quality products of international standards. The active ingredient, Solasodine glycosides (BEC), is supplied in purified form from Australian plant material utilizing Dr. Cham’s patented isolation techniques. The Curaderm-BEC5 cream product is manufactured in strict compliance with Dr. Cham’s specific ingredients and formulation as used in Phases I, II, and III clinical trials and open studies. The manufacturing of Curaderm-BEC5 is managed by a team of highly qualified pharmacists, chemists and quality conscious management.

Our manufacturing capacity can handle tens of thousands of units per week. Every unit is located in a spacious & pollution free industrial area with rich pure water sources, state of the art infrastructure along with a sophisticated laboratory for testing & analysis.
of raw materials, intermediate and finished products. Our manufacturing unit is designed for approval by Medicine control Agencies and the US –FDA with modern machinery and latest equipments.

3. Product Overview :

3.1 Current label on the Market

Specially designed after 2-decades of research by Dr. Bill Cham.
DIRECTIONS: Apply at least twice daily to clean dry skin and cover the area with a medicated paper tape. For external use only.
SUPPLEMENT FACTS:
Contains Solasodine Glycosides (0.005%)
Other ingredients: Salicylic acid, Urea.
Disclaimer: This product and its statements have not been evaluated by the FDA. This product is not intended to treat, cure or prevent any disease.
NOTE: Keep out of reach of children.
Not for use by pregnant or lactating women.
Made in Australasia
Manufactured and Distributed by Dr. Calmez Ltd
www.curaderm.net

3.2 Current Packaging on the Market

3.3. What is Curaderm-BEC5?

Curaderm-BEC5 is a topical product in a clear plastic PDHE bottle. Each product contains 20ml of formulated cream and 0.005% Solasodine Glycosides (BEC).

3.4 What is Curaderm-BEC5 used for?
The cream formulation has been shown to be effective in the treatment of the malignant human skin tumours, basal cell carcinomas, squamous cell carcinomas as well as the benign tumours, such as keratoses and keratoacanthomas.

3.5 What is the Active Ingredient?

The active ingredient in BEC5 Curaderm is a pure extract called Solasodine Glycosides. These active ingredients are extracted from Solanaceous plants such as Solanum sodomaeum, the so-called Devil’s apple, Solanum aviculare (Kangaroo apple) and Solanum melongena (Egg plant or Aubergine) which are found in the Australasia region.

3.6 What other ingredients does the product contain?

The product is a cream formulation that contains Urea, Salicylic acid which are keratolytic agents.

3.7 How much of the Curaderm-BEC5 cream does it take to treat a typical skin cancer?

On average a 20ml bottle can manage one to two large non melanoma SCC or BCC skin cancers, two to three medium sized lesions, four to eight small lesions, or twelve sun spots. The shelf life of Curaderm-BEC5 is 5 years.

3.8 Product Safety

All forms of toxicology have been investigated. Biochemical, hematological and urine analytical studies have demonstrated that there are no adverse effects on the liver, kidneys or haematopoietic system during treatment. Normal skin treated with BEC5 Curaderm, was also tested and was also free from adverse histological and clinical effects. The amount of BEC glycoalkaloids in a 20mL bottle contains the equivalent to 5 grams of extracted egg plant.

3.9 Home Based Treatment

BEC5 Curaderm is a non-toxic product as it has the same active ingredients found in egg plant which is eaten every day. Therefore you do not need to worry about any side effects or adverse reactions. Actually, the products natural attributes make the product so simple to use which greatly contributes to the products popularity.

3.10 Side Effects

Some patients experience a stinging or slight burning sensation for 10-15 minutes after each application. This is caused by the Salicylic acid and Urea in the cream.
3.11 Usual Treatment Cycle Typical Treatment Routine

The most important thing to know about using Curaderm-BEC5 is the end result is smooth, fresh skin that has a normal appearance. Stopping treatment before this point is not advised as cancer cells may still be present which will subsequently multiply.

Doctors, Naturopaths or other medical specialists can help the customer understand the process and provide important guidance. However, the product is completely safe and tested in home environments. A Health professional can book Three to Five appointments with the customer during an average BCC or SCC treatment. Two to three consultations fees can be made from sun spots and keratoses.

Sunspots and Keratoses involves applying the cream 2 or 3 times a day and within a few days the skin will appear normal again.

In the case of BCCs and SCCs, the treatment process is longer as the lesion is bigger and malignant. In this case it is very important for people to understand the process because, during treatment the lesion usually appears worse than pre-treatment.

Curaderm-BEC5 penetrates the skin tissue and moves its way around the healthy cells to find the cancer infected cells. Once these cells are located the two BEC5 actives are activated to perform their duties. The first active contains a receptor recognizing agent that has the key to the cancer cell door. Once inside, the second active finds the lysosome (stomach) of the cell and explodes the stomach, killing the cancer cell. This killing of the cancerous cells causes a slight inflammation. This can be evidenced on the skin surface through the lesion appearing bigger and possibly watery material will seep from the lesion.

There is no need to worry. This seemingly worsening of the lesion is just a sign that the cancer cells have been destroyed creating a disturbance to the skin tissue structure. In addition, Curaderm-BEC5 is seeking out and destroying cancer cells that were not observable clinically (by the bare eye). What we see with skin cancers may be the tip of the “iceberg”. Underneath the skin the cancer may be much, much larger. This is why during treatment the lesion appears to be much larger than before treatment. The dead cancer cells are replaced with healthy normal cells. Despite the increase in lesion size it is most vital that you continue to apply the Curaderm-BEC5 cream. The continued application allows more Curaderm-BEC5 to locate cancer cells in the surrounding tissue.

The BEC active literally traces and seeks out all the cancer cells. It is imperative that the lesion area is cleaned with antiseptic and an occlusive surgical tape dressing such as micropore tape is used after each Curaderm-BEC5 application. The treated lesion is not allowed to dry out and form a scab.
The objective of Curaderm-BEC5 treatment is to return your skin to be absolutely back to normal. Once the skin area has a completely new layer of skin with no more sores, inflammation or break in the skin surface, then the treatment is over. We are glad that it is easy for everyone to know when the treatment is over because everyone’s principal objective when treating skin cancer is to have skin return absolutely back to normal. Cancer free and scar free are of course also results you can expect from using Curaderm-BEC5. However, if the treated cancer was originally a very large lesion, a very small amount of scar tissue may be seen at the end of treatment.

4. Advantages of investing into the promotion and distribution of Curaderm-BEC5 in your marketplace.

4.1 Immediate Market Availability
Curaderm-BEC5 falls into the classic story of the product that was invented before its time. When Curaderm was first released on the Australian market in the 1980s the emphasis of skin cancer was just an emerging problem. Over recent decades, Government and Human interest groups have steadily promoted the awareness of skin cancer risk and consequently diagnosis in conjunction with ever increasing UV levels has spiraled the rate of skin cancer to epidemic proportions. Now, in 2006 the world urgently needs a cost effective and straightforward approach to dealing with skin cancer.

4.2 Curaderm-BEC5 is complete for the marketplace
- World wide patent – stage 4 clinical studies, the highest grade of medical research. complete (competitors would need years to catch up on research and have no chance in surpassing are 15 years of CLINICAL experience with real patients). There has been no reported health problems with treatment to this day, showing the product is safe and effective for the masses.
- Clinically proven at leading research institutions including Royal Brisbane Hospital and Royal London Hospital
- Pharmacologically active ingredient has been identified and mode of action established.
- Dosage, side effects, toxicology and all other safety elements have been confirmed
- Manufacturing production for 10,000 units every 3 days. Production is scalable upwards.
- Curaderm-BEC5 is the Only Natural treatment to battle the skin cancer epidemic. This is what will drive the company’s success. All other treatments are either toxic or surgical and cost in the thousands, which is what all customers fear.
4.3 Assistance to product and marketing needs

Our team of professional business operators, experienced in Health manufacturing, Medicine, Sales and Marketing, Administration and logistics, can assist your team to launch with minimal investment. This meaning, you can maximize return on investment with minimal set up time.

4.3.1 Sales and Marketing - We will provide a sales and marketing plan of action tailored to specific consumer markets/industries or general mass marketing through advertising. Many branding opportunities are possible. Clients have used Dr. Cham for seminars, magazine articles, web news as well as television. The company has available a huge series of content articles, medical research profiles, written content and other related information that can be incorporated within our distributors sales and marketing materials.

4.3.2 Clinical Information – Our clinical trial and customer results are available as a comprehensive guide to the treatment of non melanoma skin cancers and sun spots with Curaderm-BEC5. A wide variety of electronic and print resources are available to provide insight into treatment cycle and expectations. This complete resource means that Doctors, Naturopaths, Pharmacies and Natural health retailers who purchase from distributors are provided every piece of information to effortlessly guide patients through the Curaderm-BEC5 treatment.

4.4 Key Product Advantages

- Over 100,000 people have used Curaderm-BEC5 with absolute safety and near 100% successful results.
- Clinically proven results reflect the mode of action that as long as the product is given contact to the pre-cancerous and cancerous cells, the BEC will eliminate their existence.
- Customer can easily recognise completed treatment when skin returns to normal appearance.
- Product delivers outstanding cosmetic results by ensuring healthy skin cells are not affected by treatment and thus available to regenerate with healthy inner and outer skin health.
- Skin cancer sufferers do not usually suffer the affliction just once but several to dozens in their lifetime. Therefore, the lifetime value of the product in terms of repeat purchase and brand loyalty is outstanding.
- Customers who choose Curaderm-BEC5 are so delighted with the results, especially compared to other options, that there is very strong referral business whereby friends and family of existing customers are quickly converted to customers.
• As Curaderm-BEC5 therapy takes several weeks to complete and the lesion undergoes a variety of changes, there is excellent opportunity for Doctors and Naturopaths to guide treatment and gain consultation revenue from the patient using Curaderm-BEC5

• BEC is Eaten Every Day. Most over the counter and prescription drugs in western medicine have some type of side effect or you can expect some type of usage caution. With Curaderm, however, it is pleasing to note that humans have eaten BEC every day for hundreds of years through the consumption of eggplant (aubergine).

4.4 Photo’s of Key Product Advantages

5. Curaderm-BEC5 Medical Research Overview

Following two decades of medical research and clinical trials Curaderm-BEC5 is now recognized by leading Dermatologists and Medical Practitioners as a safe and effective therapy for non melanoma skin cancers with excellent cosmetic outcomes.

5.1 Research Milestones

These milestones summarise medical research and clinical trials on Curaderm-BEC5, previously marketed or researched under the names BEC, BEC01, BEC02, BEC05 Curaderm and Curaderm-SO.

• In 1978, Biochemist, Dr. Cham first investigated the curative properties of an Australian bush plant the “Devils Apple”. Dr Cham identified the plant to be a
member of the Solanum species. Early laboratory analysis had the initial purpose of identifying and isolating the phytochemicals within the plant responsible for the antineoplastic (anti-cancer) activity.

- At the time, Dr. Cham was a senior professional at the University of Queensland Department of Medicine.

- Dr. Cham knew that established anti-cancer agents; Vincristine and Vinblastine are glycoalkaloids. Dr. Cham discovered that there were also glycoalkaloids in the Devil’s Apple. But these glycoalkaloids were very different in structure than those found in the periwinkle plant. Once the glycoalkaloids were fully characterized Dr. Cham realized that the interest in the source material went back a hundred years in the literature.

- With the specific phytochemicals identified and extracted under a proprietary method, the chemical structure was named BEC, after the initials of inventor Bill Elliot Cham. The same active ingredient has subsequently been identified in the common eggplant or aubergine, consumed by millions on a daily basis.

- Throughout the 1980s Dr. Cham was a senior professional at the University of Queensland Department of Medicine. He built a laboratory at his house and conducted private research into the BEC mixture. Dr. Cham proceeded to investigate the active ingredients efficacy and safety through a series of laboratory, toxicology, human cell line and Animal studies.

- After years of research, Dr. Cham was able to define the specific “Mode of Action” of the BEC. The unique anti-cancer functionality of the chemical was the capacity for BEC to select between healthy and cancerous cells. The BEC – cancer specific mode of action is a first of its kind in anti-cancer breakthroughs.

- The results of these tests showed the ingredient had excellent potential for a wide selection of internal cancers. Cell culture studies showed that BEC was much more effective than various well-established antineoplastic agents (vinblastine, cisplatin, chlorambucil) and most importantly the therapeutic index (LD50/ED50) was much higher with BEC compared to the established antineoplastics (1994). The mode of action of established antineoplastics is vastly different than BEC.

- However, Dr. Cham realized that the most promising shorter term application for the natural drug would be a topical cream application containing the BEC ingredient as a treatment for skin cancer.

- Once this safety was assured Dr. Cham spent the 1990s conducting new series of research milestones. As an Academic at Queensland University, he worked closely with Royal Brisbane Hospital in Brisbane Australia and held series of clinical trials with people from the world’s Skin cancer capital.
• Clinical trials in Australia and subsequently at Ten United Kingdom Skin Cancer Clinics had the specific purpose of returning the skin to normal appearance with zero presence of cancer as defined by biopsy. All clinical trials showed a success range of 78% - 100% Success. Clinical trial participants have been followed beyond 10 years with zero recurrence reported.

• BEC is now undergoing clinical trials for internal cancer product development by Australian Biotech company Solbec Ltd. The results are promising. Further information can be found on the website – www.solbec.com.au

• Dr Cham’s work has now been confirmed by a myriad of scientists throughout the world (see website: www.curaderm.net as well as Google search: Solamargine and/or Solasonine).

7. Clinical and Medical Detail

7.1 Pharmacological Overview

• The structure of these phytochemicals were identified as glycoalkaloids consisting of Solasodine glycosides (1986).
• The solasodine glycosides were found as a mixture of triglycosides, diglycosides and monoglycosides. Dr. Cham patented and termed the specific mixture of these glycoalkaloids BEC.
7.2 Mode of Action of BEC – 1990

Dr. Cham discovered and described a novel Mode of Action of BEC in selectively destroying cancer cells without harming normal cells (1990).

- Specific endogenous endocytic lectins (EELs) were found to be present at much higher concentrations in cancer cells relative to normal cells.
- These EELs were present on the cell surface as receptors which recognized and bound the sugar moiety, in particular the rhamnose sugar (1990).
- BEC was subsequently internalized in the cancer cell and became lysosomotropic and consequently autolysis occurred.
- The disintegrated lysosome resulted in apoptosis of the affected cancer cells.
- BEC was also shown to induce cell apoptosis by modulating tissue necrosis factor (TNF) (2004).

Above: Diagram demonstrates the Mode of Action on Cancer Cells
7.3 The Curaderm carrier cream - formulated with carrier agents to reach cancer infected cells deep in the skin tissue.

Dr. Cham's intricate knowledge of BEC technology & the specific pharmacology of Solasodine glycosides makes Curaderm-BEC5 a most effective treatment for non melanoma skin cancer. This Research & Development assured an effective delivery system for the BEC to reach all the cancer cells and disintegrate their existence.

**Active Ingredient Principles**

The active ingredient, BEC has to be in direct contact with cancer cells to effectively kill them. This means the active must penetrate below the skin surface, the Curaderm-BEC5 carrier cream has been scientifically formulated to reach and eliminate the existence of cancer cells deep within the skin tissue.

**100% Effective Carrier Cream**

Research and Development for a 100% effective BEC carrier cream, has been as fundamental as discovering the cancer killing active. Dr. Cham tested absorption levels of hundreds of creams, ointments, lotions and gels. The creams ranged from simple everyday moisturisers to exotic ingredients such as natural mucopolysaccharides, synthetic compounds, unique surfactants and many others.

This R&D lead to the invention of a uniquely formulated cream. The other important element in choosing an appropriate carrier cream was that certain important sugar agents can easily break off the glycoalkaloid active when mixed with ingredients of standard lotions resulting in the inactivation of the anti-cancer agent BEC. Virtually all everyday creams make the glycoalkaloid inactive against cancer cells. The Curaderm carrier cream is designed to be the perfect delivery mechanism to deliver the active throughout the skin dermis locating and dissolving all the cancer cells.

The Curaderm cream has been subject to a series of R&D stages lasting over two decades. This research was focussed on finding the ideal formulation that the active could reach & destroy every cancer cell deep into the pores. The results have been scientifically published and recommended as a reliable and safe treatment by researchers worldwide including the most recent Phase 3 clinical trials and open studies by United Kingdom Hospitals. Decades of clinical results prove Curaderm-BEC5 can ensure cancer and pre-cancerous destruction both on the surface and within the dermal layer.
7.4 Safety Data

Dr Cham's prime concern has always been the product safety. Over a decade was devoted to designing a powerful yet completely safe formulation. Results time and time again show consistently that Curaderm and its active ingredient, BEC, when used according to the manufacturers instructions is completely safe and-

- Non toxic
- Non mutagenic
- Does not affect the heartbeat or blood flow.
- Biochemical, haematological and urinanalytical studies demonstrated that there were no adverse effects on the liver, kidneys or haematopoietic system (blood cells) during and after treatment.

BEC has the same safety profile as solanine, the glycoalkaloid found in the potato, which is present in potato chips and consumed worldwide. Eggplant or aubergine (Solanum melongena) has been examined, and has been shown to contain the exact replica of BEC. This means that a fruit, which is eaten as a vegetable throughout the world, contains BEC in less concentrations than a finished bottle of Curaderm-BEC5.

100,000 people have successfully treated their skin cancers with Curaderm achieving excellent cosmetic results without any adverse reactions.

The non invasive and non toxic advantage of Curaderm-BEC5 contrast sharply with the limitations consistent across all commonly used skin cancer treatments such as:

- Formation of scar tissue.
- Lack of normal tissue regrowth i.e loss of skin tissue.
- Limited access to cancer that exists within the lesion if it is deep within the skin.
- A high rate of recurrence of the skin cancer.

7.5 Human Clinical Trials

- Solasodine glycosides (BEC) had confirmed antineoplastic activity in cell lines, animals and humans. Four series of clinical trials demonstrated that the Solasodine glycosides at 0.005% BEC into a cream formulation was effective in the treatment of keratoses, BCCs and SCCs.
- Stage one and two clinical trials were conducted with the Royal Brisbane Hospital in Australia.
- All clinical trial lesions were diagnosed by histopathology and once the skin returned to usual appearance punch biopsies showed complete clinical and histological regression and that the BCCs, SCCs or Keratoses were no longer present.
- Follow up periods for up to ten years revealed there were no recurrences of the skin cancer.
• Subsequently a multicentre study involving 10 independent centres in the United Kingdom conducted a Double-blind, Vehicle-controlled, Randomised, Parallel Group Study to Assess the Efficacy and Safety of [Curaderm] BEC-5 in the Treatment of Patients with Basal Cell Carcinoma. With this study the cut off treatment period was 8 weeks. Follow up period was 12 months.

• In this study efficacy was defined as: Complete healing of index lesion (before treatment at least 0.5cm in diameter) after 8 weeks ± 3 days, confirmed by histological report from 2mm skin punch biopsy taken from the periphery of site lesion.

• Lesion was clinically healed when site became replaced by normal smooth skin and a skin biopsy of the treated area confirmed that no neoplasia remained at site. Response to treatment confirmed by histology report is shown in the following Tables;
These studies were conducted for eight weeks. Similar observations were done by Dr Cham in his initial studies when the eight week period of treatment was completed. However, in the case of Dr Cham studies treatment continued up to 13 weeks and it was shown that 100% of all lesions were successfully treated. Thus, it stands to reason that if the Multi Centre studies had continued to 13 weeks they too would have observed a 100% success rate.

8. Research Appendix

Below you will find excerpts from Published Medical and Clinical research results from 1987 to 2002 on the performance of Curaderm-BEC5 as an effective non melanoma skin cancer treatment. These research and clinical breakthroughs were headed by Dr. Bill Elliot Cham.

**Antitumour Effects of Glycoalkaloids Isolated from Solanum sodomaeum L.**
Planta Med. 53, 34-36.

**Solasodine glycosides. Selective Cytotoxicity for Cancer Cells and Inhibition of Cytotoxicity by Rhamnose in mice with sarcoma 180**
Cancer Letters, 55, 221-225.

**Solasodine glycosides. In vitro preferential cytotoxicity for human cancer cells.**
Daunter B, Cham, B.E

**Topical treatment of pre-malignant and malignant skin cancers with Curaderm**
Drugs of Today 26, 55-58.

**Topical treatment of malignant and premalignant skin lesions by very low concentrations of standard mixture (BEC) of solosadine glycosides.**
Cham, B.E, Daunter B and Evans, R.A
Cancer letters 59, (1991) 183 - 192

**Solasodine glycosides as Anti-cancer Agents. Pre-clinical and Clinical studies.**
Asia Pacific Journal of Pharmacology. 9, 113-118.

**CLINICAL APPRAISAL ON RESULTS FROM PHASE III Clinical Trials and OPEN STUDIES FROM ROYAL LONDON HOSPITAL 2002**

Dr Sangeeta Punjabi MBBS DVD DipNB (Dermatology)
Research Registrar, Royal London Hospital

Rino Cerio BScFRCR (Lond) FRCP (Edin)
Consultant Dermatologist and Senior Lecturer in Dermatopathology
Standard mixture of triglycosides solasonine [(22R, 25R)-spiro-5-en-3β-yl-α-L-rhamnopyranosyl-(1→2)α-D-glucopyranosyl-(1→3)β-D-galactopyranosyl], solamargine [(22R,25R)-spiro-5-en-3β-yl-α-L-rhamnopyranosyl-(1→2)α-D-glucopyranosyl-(1→4)β-D-glucopyranosyl] and their corresponding di- and monoglycosides

Curaderm®
Curaderm® SO®
N = 142–113
Antineoplastic
INTRODUCTION

Plant Kingdom and Drugs

The plant kingdom has supplied us with some excellent drugs. Pain sufferers appreciate the relief provided by morphine. Victims of congestive heart failure appreciate the life-saving role of digitoxin or digoxin. Migraine patients experience the dramatic relief effected by ergotamine. Children with leukaemia have recognised the improvement of their condition by treatment with vincristine.

In addition, the natural plant drugs have served as useful prototypes for even better medicines. Synthetic chemists have been able to convert morphine to hydromorphone, lysergic acid to methysergide, cocaine to procaine, physostigmine to neostigmine and even salicin to aspirin. The list could go on and on.

Glycoalkaloids Derived from the Plant Kingdom

The current study addresses steroidal alkaloid glycosides or glycoalkaloids which are also derived from the plant kingdom. In particular, the glycoalkaloids described in this study are found as constituents of many solanaceous plants and their fruits, some of which are edible, including, for example, the aubergine (egg plant). The functions of these glycoalkaloids are largely unknown. These glycoalkaloids consist of the alkaloid solasodine which is conjugated with specific sugars. Solasodine is a very important source of raw material for the synthesis of steroid drugs (e.g. cortisone and progesterone).

BEC – The Glycoalkaloids used in the Current Study

BEC is a standard mixture of triglycosides solasonine [(22R, 25R) - spiro-5-en-3β-yl-α-L-rhamnopyranosyl-(1->2gal)-O-β-D-glucopyranosyl-(1->3gal)-β-D-galactopyranose] (33%), solamargine[(22R25R)-spiro-5-en-3β-yl-α-L-rhamnopyranosyl-(1->2glu)-O-α-L-rhamnopyranosyl - (1->4glu)-β-D-gluco-pyranose] (33%), and their corresponding di- and monoglycosides (34%) (1 – 4). All the glycosides contain the same aglycone, solasodine (1,4).
Antitumour Effects of Glycoalkaloids Isolated from Solanum sodomaeum

Bill E. Cham¹,², Merv Giffen³ and Linda Wilson⁴

Received: May 14, 1986

Abstract: Glycoalkaloids extracted from Solanum sodomaeum L. show antineoplastic activity against Sarcoma 180 in mice. Approximately 33% of the total glycoalkaloid content consisted of the triglycoside solasonine and 33% of the triglycoside solamargine. The remainder was a mixture of mono- and diglycosides in which the aglycone was solasonine. Single dose studies of these glycoalkaloids with mice containing Sarcoma 180 indicated that the \( ED_50 \) was 9 mg/kg, whereas the \( LD_50 \) was 30 mg/kg resulting in a therapeutic index of 3.3. Single dosages of 8 mg/kg given on two consecutive days resulted in inhibition of tumour progression with greater than 40% survival. In contrast, the use of the same dosages given on three or four consecutive days resulted in greater than 90% survival.

Introduction

Extracts from plant material have been used to treat cancers for centuries. Examinations of such extracts have resulted in the identification of well established antineoplastic agents such as vincristine. It has also been reported that extracts from the Solanum species are effective in treating cancers (1). More recently, the glycoalkaloid B solasodine which is extracted from S. dulcamara was shown to possess antitumor properties (2). In a previous paper it was reported that S. sodomaeum L. contains a mixture of glycoalkaloids, the aglycone which is present in all the glycoalkaloids is solasonine (3). This communication shows evidence that these glycoalkaloids are effective against Sarcoma 180 activity in mice. Some toxicity studies of these glycoalkaloids are also presented.

Materials and Methods

Mice

Herston Whites were obtained from the Medical School, University of Queensland. Mice with a body weight of approximately 30 g and aged 8–10 weeks served as recipients. Twelve mice were randomly chosen for each experimental group.

Rats

Sprague Dawley with a body weight of approximately 275 g and aged 10–12 weeks were used in some toxicity studies. The rats were also obtained from the Medical School as above. Six rats were randomly chosen for each experimental group.

¹ Department of Medicine, University of Queensland, Clinical Sciences Building, Royal Brisbane Hospital, Queensland, 4029, Australia.
² Address for correspondence.
³ Department of Veterinary Pathology, University of Queensland, St. Lucia, Queensland, 4067, Australia.
⁴ Municipality College, Fernberg Road, Rosalie, Queensland, 4064, Australia.

Tumour

The tumour was Sarcoma 180. It was established in the ascitic fluid of Herston Whites in 1969 at the Medical School as above, and was passaged by i.p. transplantation. Tumour cells (5 x 10⁷) inoculated i.p. caused a mortality of 100% per cent with a median survival time of 23 days in the control groups.

Drugs and treatment schedules

Glycoalkaloids were extracted from the fruit of S. sodomaeum essentially as described earlier (3). The triglycosides solasonine and solamargine were present at similar concentrations, representing 57% of the total extracted glycoalkaloids. The remainder consisted of a mixture of di- and monoglycosides. The aglycone of all the glycoalkaloids was solasonine (3). In the present studies, the extract containing the mixture of these glycoalkaloids was investigated. A solution of 0.5 g glycoalkaloids (100 ml dimethyl sulfoxide (DMSO)) was used. The glycoalkaloids in DMSO, now referred to as BEC 01, were administered i.p. in concentrations ranging from 0.1 to 100 mg/kg animal weight. In the efficacy studies, the dose of BEC 01 was given 0.5 h after administration of the Sarcoma 180 tumour cells.

Coronarivus parvum (CPS)

Killed vaccines of this bacteria (Wellcome Foundation, Sydney, Australia) were kindly provided by Dr. K. Donald of the Royal Brisbane Hospital. Thirteen aliquots of the suspension (7 mg/ml, dry weight) were injected i.p. in mice.

Pneumococcal (PHA)

PHA (purified) was purchased from Wellcome Foundation, Sydney, Australia. A suspension of 7 mg PHA/ml saline was used in these studies. Thirty aliquots of this suspension were injected i.p. in mice.

Results

The results obtained with the lethal toxicity tests of BEC 01 in mice are shown in Fig. 1. Single i.p. doses of 15 mg/kg produced toxic deaths and the \( LD_{50} \) was 30 mg/kg. All the mice died after single i.p. doses over 35 mg/kg. In rats the \( LD_{50} \) for a single i.p. dose of BEC 01 was 41 mg/kg. The \( LD_{50} \) for a single dose by gastric intubation in mice was 550 mg/kg.

Toxicity studies with multiple i.p. doses indicated that the \( LD_{50} \) for mice by 14 daily single i.p. administrations was 10 mg/kg. The \( LD_{50} \) for rats by 8 i.p. administrations over 8 days with one injection per day was 20 mg/kg.

The most critical time for the animals was the first 48 h after administration of BEC 01. If the animals survived the BEC 01 treatment during the first 48 h, they then continued to live an apparently normal life.

Fig. 2 illustrates the effect of single doses of varying concentrations of BEC 01 on the absolute survival of mice which had the Sarcoma 180 tumour. Single doses of concentrations up to 8 mg/kg did not have any effect on the survival time. Some mice survived the Sarcoma 180 with a single dose of between 8 and
Solosadine glycosides. Selective cytotoxicity for cancer cells and inhibition of cytotoxicity by rhamnose in mice with sarcoma 180

B.E. Cham and B. Daunert

*The University of Queensland Departments of Medicine and *The University of Queensland Department of Obstetrics and Gynaecology, Clinical Sciences Building, Royal Brisbane Hospital, Herston, Queensland 4006 (Australia)

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Summary

BEC, a standard mixture of solosadine glycosides is effective in vivo against murine sarcoma 180 (S180), whereas the aglycone solosadine at equimolar concentrations is ineffective. The efficacy of BEC against S180 in vivo can be inhibited by rhamnose. Mice which are in the terminal stage with S180 can tolerate and become symptom-free of cancer by single dose administration of BEC at concentrations of BEC three times the LD_{50} for normal mice. These observations suggest that the binding of solosadine glycosides on tumour cells may be mediated through the monosaccharide rhamnose, which forms part of solosadine, solamargine and di-glycosides of solosadine in BEC. Furthermore, these results provide evidence that BEC selectively destroys tumour cells relative to normal cells in vivo.

Keywords: solosadine glycosides; BEC; cytotoxic; sarcoma 180; in vivo

Introduction

Solosadine glycosides have antineoplastic activity in cell culture [1-3], animals [1,2,4,5], and in humans [1,2,6,7]. Cham and Evans, unpublished data. It has been demonstrated that specific endogenous lectins which are present on the plasma membranes of susceptible cells recognize and bind the sugar moiety of the solosadine glycosides [2,3]. The glycosides are subsequently internalized and cause cell death [2,3].

It was previously shown that a standard mixture of solosadine glycosides (BEC) [8] is effective in vivo against murine S180 [1,2,4]. In such studies, BEC was injected in single and multiple doses up to 4 days after administration of S180 [4]. Rhamnose is not found in mammalian glycoconjugates but forms part of solosadine, solamargine and di-glycosides of solosadine in BEC. It was considered that specific receptors for this sugar may be present on cancer cells (absolutely or in greater abundance) relative to normal cells. If these receptors exist, rhamnose would be expected to inhibit the cytotoxic effects of BEC. Here we show that rhamnose inhibits the efficacy of BEC, and that the aglycone solosadine is not effective against murine S180.

It was previously shown that mice which were
Soladodine glycosides. In vitro preferential cytotoxicity for human cancer cells

B. Daunier* and B.E. Cham

*The University of Queensland Department of Obstetrics and Gynaecology and †The University of Queensland Department of Medicine, Clinical Sciences Building, Royal Brisbane Hospital, Herston, Queensland 4006 (Australia)

(Received 22 August 1990)  (Revision received 11 October 1990)  (Accepted 12 October 1990)

Summary

Soladodine (\((R,25)-\text{spiro} 5\text{-en} 3\text{\(\beta\)}-\text{glyceroxyphosphoryl} 1\text{-trimethylammonium} 2\text{-glucopyranose} \)) is a glycoside of soladodine preferentially inhibits the uptake of initiated thymidine by cancer cells. In contrast, soladodine at equivalent concentration, and the mono- and diglycosides of soladodine have a limited effect on the uptake of initiated thymidine for other cell types. Inclusion of unstimulated lymphocytes and lymphocytes stimulated with Con A, in contrast to soladodine glycosides do not inhibit the uptake of initiated thymidine by lymphocytes stimulated with PHA or PWM. The inhibition of initiated thymidine uptake by soladodine and the mono- and di-glycosides of soladodine are dependent upon their cellular uptake by endogenous endocytic lectins (EELs). The mode of action of the soladodine glycosides, in particular soladodine, appears to be the induction of cell lysis, as determined by morphological examination.

Keywords: soladodine glycosides; BEC; cytotoxic; endogenous lectins; human cancer cells; in vitro

Introduction

Soladodine glycosides have been isolated and purified as a mixture: soladodine (33%), solasonine (33%) and di- and monoglycosides (34%) [12]. This mixture (BEC) [7] of soladodine glycosides has been shown to be effective in vivo against murine sarcoma S180 [10] and human skin cancers [8, Cham, B.E. and Daunier, B., unpublished data, 11]. However, these glycosides have not been assessed for their potential use in the treatment of other human cancers or their mode of action established. An in vitro study was therefore undertaken to determine the relative cytotoxic activity and mode of action of the mixture of soladodine glycosides (BEC) compared to other commonly used cytotoxic drugs. In addition, consideration has been given to the mechanism of cellular uptake of the soladodine glycosides. The carbohydrate moieties (glycone) of the soladodine glycosides may interact with endogenous endocytic lectins (EELs) and therefore inhibitory studies with carbohydrates have been undertaken.

Interest in plasma membrane endogenous lectins has gained momentum. The first endogenous membrane bound lectin to be identified was the asialoglycoprotein receptor on mammalian hepatocytes with specificity for galactose [1,33]. Interaction of the asialoglycoprotein (ligand) with the receptor results in endocytosis of the complex, the lectin receptor is returned to the cell surface, while the
TOPICAL TREATMENT OF PRE-MALIGNANT AND MALIGNANT SKIN CANCERS WITH CURADERM

Bill E. Cham\(^1\) and Brian Daunter\(^2\)

\(^1\)Dept. of Medicine and \(^2\)Dept. of Obstetrics and Gynaecology, University of Queensland, Royal Brisbane Hospital, Herston, Australia

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Introduction
To have a suntan has become fashionable in the last 60 years, and people have increasingly felt that exposing their skin to the sun is a healthy, happy thing to do. However, the ultraviolet part of the electromagnetic spectrum produced by the sun as light, in particular U.V.-B (320-290 nm), is responsible for producing long-term solar skin damage (keratosis) and skin cancers.

Curaderm, a topical preparation of a mixture of solasodine glycosides (SGC) which are present in some solanaceous plants, has become available to Australian practitioners for the treatment of cutaneous solar keratoses, basal cell carcinomas (BCCs) and squamous cell carcinomas (SCCs). This review covers the etiologies of keratosis, BCC and SCC, the currently available treatments, and discusses the particular attributes of Curaderm within these concepts of pathogenesis and therapeutics.

Keratosis
An overgrowth of the epidermis forms a scaly layer on the skin. The start of this lesion is usually a small patch of dilated capillaries several millimeters in diameter. Then a dry, rough, adherent yellow or dirty brown scale forms, which may bleed if picked off. It may eventually become thick and horny, with a sharp, clear division between the keratosis and normal skin. Solar keratoses occasionally regress if sun exposure is stopped before they become too established. Although non-malignant, they are potentially malignant and can develop into cancer.

Basal Cell Carcinoma (BCC)
A BCC is a malignant tumor that rarely spreads to distant sites (metastasises). It starts in the basal layer of cells, between the basement membrane and the subsequent layer of cells, and grows upwards from these. It consists of immature cells and has an organized complex of supporting tissue around it. The primary cause of BCC is sunlight (U.V.-B) on sensitive skin. Contributory causes are radiation damage, exposure to arsenic, burn scars and vaccination marks. BCCs are the most common malignant skin tumors in humans; they do not spread by metastases, but they erode tissue, and if not treated may eventually kill. BCCs may appear in a variety of guises. On first appearance, they are commonly small, rounded lumps with a pearly edge, and a thin surface covering with a few superficial transparent
Topical treatment of malignant and premalignant skin lesions by very low concentrations of a standard mixture (BEC) of solasodine glycosides

B.E. Cham\textsuperscript{a}, B. Daunter\textsuperscript{b} and R.A. Evans\textsuperscript{c}

\textsuperscript{a}Department of Medicine, \textsuperscript{b}Department of Obstetrics and Gynaecology, The University of Queensland, Clinical Sciences Building, Royal Brisbane Hospital, Queensland 4029 and \textsuperscript{c}Acacia Arcade, Acacia Ridge, Queensland 4110 (Australia)

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Summary

A cream formulation containing high concentrations (10\%) of a standard mixture of solasodine glycosides (BEC) has been shown to be effective in the treatment of malignant and benign human skin tumours. We now report that a preparation (Curaderm) which contains very low concentrations of BEC (0.005\%) is effective in the treatment of keratoses, basal cell carcinomas (BCCs) and squamous cell carcinomas (SCCs) of the skin of humans. In an open study, clinical and histological observations indicated that all lesions (56 keratoses, 39 BCCs and 29 SCCs) treated with Curaderm had regressed. A placebo formulation had no effect on a smaller number of treated lesions. Curaderm had no adverse effect on the liver, kidneys or haematopoietic system.

Keywords: topical treatment; solasodine glycosides; BEC; basal cell carcinoma; squamous cell carcinoma; keratosis

Introduction

Previous studies have demonstrated that a cream formulation containing 10\% of a standard mixture of purified solasodine glycosides (solanargine 33\%, solasonine 33\% and diand monoglycosides 34\%), referred to as BEC [1], was effective clinically and histologically in the treatment of human malignant skin tumours; BCCs, SCCs and benign tumours; keratoses and keratoacanthomas. In such studies [1—4] it was shown that there was no recurrence of any of the skin tumours after a 3—6-year follow-up period [2]. Some patients in the previous study [2] have now been followed up for up to 10 years and no recurrence of the treated lesions have been observed (unpublished results). These results compare favourably with modalities of treatment such as surgery, radiotherapy and dermatology which have certain limitations such as formation of scar tissue, lack of normal tissue regrowth, limited access to the lesion if it is deep within the skin and a high rate of recurrence [4].

BEC is cytotoxic and selectively kills cancer cells [1—6]. Specific endogenous endocytic lectins which are present on the plasma membranes of susceptible cells recognize and bind
I. Introduction

There is a resurgence in the interest of solasodine-containing species of Solarium. Previously most of the interest of solasodine-bearing plants was due to their potential conversion to synthetic drugs. However, more recently it was shown that some biological activity of the original glycosides is present. Certain solasodine glycosides have been shown to have anti-cancer properties. The alkaloid solasodine on its own does not appear to be antineoplastic. The solasodine has to be conjugated to specific sugars in order to possess the anti-cancer properties. An equally important observation was recently reported. Endogenous endocytic lectins (EELs) which are endogenous sugar receptors have been biochemically characterized in tumours. There are qualitative as well as quantitative differences in histochemical patterns of certain carbohydrate binding proteins in tumours. Solamargine a naturally occurring solasodine triglycoside binds to the EELs and this interaction initiates a chain of events, resulting in the internalization of solamargine with concomitant delivery of solasodine to the targeted cell. Solamargine travels via the desmosomes to the lysosome. The action of solamargine is lysosomotropic (rupturing of the lysosome). These events result in sudden cell death. The efficacy of solamargine for killing cancer cells depends on the specificity of receptors on these cells for the recognition of solamargine. In this review, attention is drawn to solasodine glycosides and their actions on cancer cells relative to normal cells.

II. Solasodine Glycosides

Diosgenin was the most important source of raw material for the synthesis of steroid drugs. Because the supplies of diosgenin was limited (1), a search for alternative raw materials was motivated. Solasodine, which is chemically very close to diosgenin has since replaced diosgenin. Indeed, solasodine, a nitrogen analogue of diosgenin is reported to be the sole source of cortisone and progesterone (2). Thus there is much information on the aglycone solasodine but less information on the naturally occurring conjugate solasodine glycosides.
Tuesday, April 22, 2002

Dear Sirs,

Clinical Appraisal of BECS

You have requested us to detail our clinical experience with BECS in the treatment of malignant lesions of the skin. We understand that this may be shown to potential purchasers of or its interest in the BECS project.

Background

The Dermatology Department at the Royal London Hospital has acted as an approved and designated center in two clinical trials to determine the safety and efficacy of BECS cream in the treatment of cutaneous lesions of the skin. In the first of these, a pivotal double blind randomized study, Royal London recruited, treated and monitored 21 of the 94 patients. In the second trial, comprising 41 patients, Royal London was the sole designated centre. This trial was an open study, conducted primarily to assess the safety of the product. Hereewith we summarize our observations on use, safety, efficacy, cosmetic results and resource effectiveness of the product.

Use

The trials were formally restricted to patients diagnosed by physician as having superficial basal cell carcinomas. Hence patients with morphoeic lesions were excluded. However, subsequently conducted punch biopsy results demonstrated that several trial patients did in fact have invasive basal cell carcinomas. Even so, our findings in respect of these patients were that successful treatment of the invasive form of basal cell carcinoma paralleled the general success rate of BECS, i.e. around 78%.

In our view these results, in the least, justify a more extensive clinical trial of BECS against such cancers. We note in this respect that treatment of the morphoeic form of the affliction is presently confined to surgical removal. We are not aware of any emerging therapy, for example, photodynamic therapy that has the potential to extend to treatment of other than superficial skin cancers.

Safety

Our clinical experience has shown that BECS is safe. In the two trials frequent (twice daily) and prolonged (8 weeks) application of a cream incorporating BECS under occlusive dressing resulted only in local skin irritation and erythema. Very few patients under our supervision withdrew from treatment on this account. Hence we consider treatment with BECS to be a safe therapy.

Furthermore, patient blood and urine was analyzed using very sensitive methods to determine the presence of the BECS during and after a standard treatment regime (twice daily for 8 weeks). Such analysis produced no evidence of the active pharmaceutical ingredients in BECS or their breakdown products. Hence it was concluded that there is no systemic absorption of BECS. This is extremely important from the clinical perspective and may be contrasted with other topical preparations. For example, 5 Fluorouracil shows systemic absorption and can prove to be toxic when used with large lesions.

The Royal Hospital of St. Bartholomew, The Royal London Hospital. The London Chest Hospital. The Queen Elizabeth Children’s Service.

Lead Clinician: Dr David Payne
General Manager: Malcolm Newton
Efficacy

Royal London has a large dedicated skin cancer clinic as it is a Skin Cancer Center for the North East Thames Network. This fact, coupled with the results of the first trial, was instrumental in Royal London’s conduct of the second open study. Success rates in this open trial paralleled the multi-center efficacy rate of 78%. Success was defined as zero presence of basal cell carcinoma after histological examination of samples extracted from the lesion site by punch biopsy.

We consider that this rate of treatment success more than justifies the physician considering BECS as an alternative to currently predominant treatments such as surgical excision or cryotherapy.

Cosmetic Evaluation

BECS results in ulceration of the lesion site during treatment. However, we have observed that post treatment the wound is quickly replenished with normal tissue and that residual scarring is minimal. Whether such scarring proves more or less extensive than that consequent upon surgical excision is dependent upon a number of factors including lesion size, location and so on. However, it can be said that the cosmetic results offered by treatment with BECS are comparable to that resulting from surgical excision.

Resource Effectiveness

Basal cell carcinoma is a slow growing, locally invasive malignant skin tumor which mainly affects Caucasians. Dermatologists, plastic surgeons and radiotherapists jointly manage the affliction. Such management usually involves surgery. The risks of surgical intervention are well known.

Moreover, excision of basal cell carcinoma from the facial area often involves reconstructive surgery, which can be both time consuming and costly. Hence an alternative, safe and efficacious method of treatment of basal cell carcinoma that does not require physician or hospital attendance must be encouraged.

In our view and experience BECS is a topical preparation, which is safe and effective, ideal therapy for outpatient treatment. Hence BECS is a much needed alternative to surgery for basal cell carcinoma. This is the commonest cancer in Caucasians worldwide and the prevalence continues to increase with an increasing ageing population.

It is a cost effective treatment for both primary and secondary skin cancer care.

We trust that the foregoing is adequate for your purposes.

Yours sincerely,

Rino Cerio BScFRCP(Lond) FRCP(Edin)
FRCPATH Consultant Dermatologist and
Senior Lecturer in Dermatopathology

Dr Sangeeta Punjaisi MBBS, DV, DipNB
(Dermatology) Research Registrar, Royal
London Hospital
United Kingdom Dermatologist
Phase 3 Clinical Trials and Open Studies, U.K Hospitals, 2002

CLINICAL APPRAISAL ON RESULTS FROM PHASE III Clinical Trials and OPEN STUDIES FROM ROYAL LONDON HOSPITAL

Dr Sangeeta Punj abl
MBBS Research Registrar, Royal London Hospital
DVD DipNB (Dermatology)

Rino Cerio
BScFgRCP (Lond) FRCP (Edin)
Consultant Dermatologist and Senior Lecturer in Dermatopathology

Background

The Dermatology Department at the Royal London Hospital has acted as an approved and designated centre in two clinical trials to determine the safety and efficacy of BEC5 cream in the treatment of cancerous lesions of the skin. In the first of these, a pivotal double blind randomized study; Royal London recruited, treated and monitored 21 of the 94 patients. In the second trial, comprising 41 patients, Royal London was the sole designated centre. This trial was an open study, conducted primarily assess the safety of the product. Herewith we summarize our observation on the use, safety, efficacy, cosmetic result and resource effectiveness of the product.

USE

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considering BECs as an alternative to currently predominant treatment such as surgical
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care.