

## MediHerb - The Company

MediHerb is an Australian owned company based in a beautiful agricultural area of Queensland. In our pharmaceutical GMP manufacturing facility we produce a large range of herbal products in liquid extracts and tablets. The mission of the company is to provide superior quality efficacious products to health care professionals.

Co-founded in 1986 by Associate Professor Kerry Bone, MediHerb is the first choice for health care professionals in herbal products in the United States, Australia, New Zealand, South Africa and the United Kingdom.



## Total Commitment to Quality

The philosopher and teacher Rudolf Steiner once said, “For every human illness, somewhere in the world there exists a plant which is the cure. I believe that there is a healing potential locked inside plants which is integral with their evolution, just as it is part of human evolution to learn to tap this wonderful gift of Nature.”

In the words of MediHerb’s Co-Founder, Associate Professor Kerry Bone: “Our passion at MediHerb is to unlock the healing power of plants by combining the time-honored wisdom of traditional knowledge with sound clinical experience and the rigor of scientific research. This quest can only be attained by the total commitment to quality and continuous improvement, which permeates every aspect of our endeavors”.

## The Health Professional’s Company

A key part of MediHerb’s success is that it recognizes the importance of having health professionals in key areas of the organization – over 20 naturopaths and master herbalists have roles within new product development, technical writing, laboratory, clinical support and senior management. These health care professionals, including Kerry Bone, continue to see patients in their own clinics every week keeping them in touch with current health issues. This means that we know from our own hands-on experience how the MediHerb products work and can provide health care professionals and their patients with guidance and education.



Over 20 naturopaths and master herbalists within MediHerb

## Redefining Quality

MediHerb’s commitment to quality is evidenced in every aspect of our business, from the rigorous sourcing and testing of herbs and the in-depth research and development of herb active constituents and therapeutic applications, to the development of manufacturing and extraction processes that have revolutionized the herbal products industry. In 20 years of operation, MediHerb has not only demonstrated an unwavering commitment to quality in herbal products, we have redefined it. We believe that our approach to quality sets a standard for herbal products that is unsurpassed in the world today.

## Quality Issues with Herbs

Working with herbs to consistently manufacture high quality products is not easy as plants are naturally complex and the quality of a finished product can vary enormously, presenting MediHerb with continual challenges. These challenges are numerous, and include the inherent biological and chemical variability of herbs, the influences on quality of growing, harvesting, drying and storage, extraction of the herb, stability and the ultimate problem of defining quality in a meaningful way.

Put simply not all herbal products are the same

Not all herbs contain the same levels of active constituents. Not all herbs are grown or harvested or dried or stored in the same way. Not all herb growers', suppliers', or manufacturers' standards are the same and not all methods to determine quality are the same.

## Sourcing of Herbs

MediHerb is the largest purchaser and processing plant of herbs in Australia and since the beginning we have actively sought the best quality herbs from around the world. Our long-standing relationships with herb growers include technical assistance on how best to grow herbs. This includes information on:

- Varietal selection
- Climatic and soil requirements
- Time of harvest
- Harvesting techniques
- Drying parameters
- Storage requirements post-drying
- Providing feedback to growers on herb quality

By working with herb growers in this way, we have been able to increase the level of knowledge and awareness of issues affecting herb quality.



Wherever possible we aim to source organically grown and wildcrafted herbs, and also work with growers to help cultivate endangered species, for example Golden Seal. We are very fortunate in Australia to have healthy soils and a wonderful climate for herb growing, so many of the herbs used in MediHerb products are from local growers. We also source herbs from overseas where the climatic conditions and specific handling requirements are the optimum, for example Devil's Claw from the Kalahari Desert and Cat's Claw from Peru. It is particularly important for these indigenous communities who depend on the income of the herb crops for their well-being that they understand the quality issues and how best to grow or sustainably harvest the herb. Together we can ensure that they will sell their crops and provide income for their community.

## Our Policy on Endangered and Threatened Medicinal Plants

MediHerb takes steps to avoid medicinal plants becoming classified as endangered species and has developed a system of identifying and classifying the 'threat' to particular herbs. 'Threatened' is not an official classification, it is determined by MediHerb based on information received from independent, reliable sources such as CITES (Convention on International Trade in Endangered Species of Wild Fauna and Flora), TRAFFIC (Wildlife Trade Monitoring Network) and United Plant Savers.

When a wildcrafted herb is classified as 'threatened' by MediHerb, steps are taken immediately to find alternatives to overcome or reduce the threat.

Listed below are guidelines MediHerb has developed to reduce the threat of extinction of medicinal plants:

1. Where the threatened status of an herb is specific to a region or country, MediHerb does not acquire the herb from that region or country, eg Uva Ursi in parts of South-East Europe
2. MediHerb uses cultivated herb sources of threatened herbs, where available, eg our Golden Seal is always from a cultivated source
3. Where no cultivated source is available, MediHerb seeks to establish cultivation in conjunction with herb growers, eg Black Cohosh and False Unicorn Root
4. If 2 and 3 are not options, MediHerb then investigates the wildcrafting techniques and protocols to ensure they are conducted sustainably and ethically, eg Devil's Claw
5. In certain cases, substitution of the threatened herb with a medicinally interchangeable species will be possible. This option requires technical and Research and Development involvement, eg Arnica
6. MediHerb actively promotes using alternate herbs in place of endangered herbs by educating health professionals, eg using Shatavari and Wild Yam rather than False Unicorn
7. Where a threatened or endangered herb is part of a tablet or liquid formulation, MediHerb will reformulate the product to include a different herb
8. When an herb is listed in CITES appendix II and a cultivated source is not available, MediHerb ceases to use that herb and deletes the product from the range, eg Pygeum



*Arctostaphylos uva-ursi*

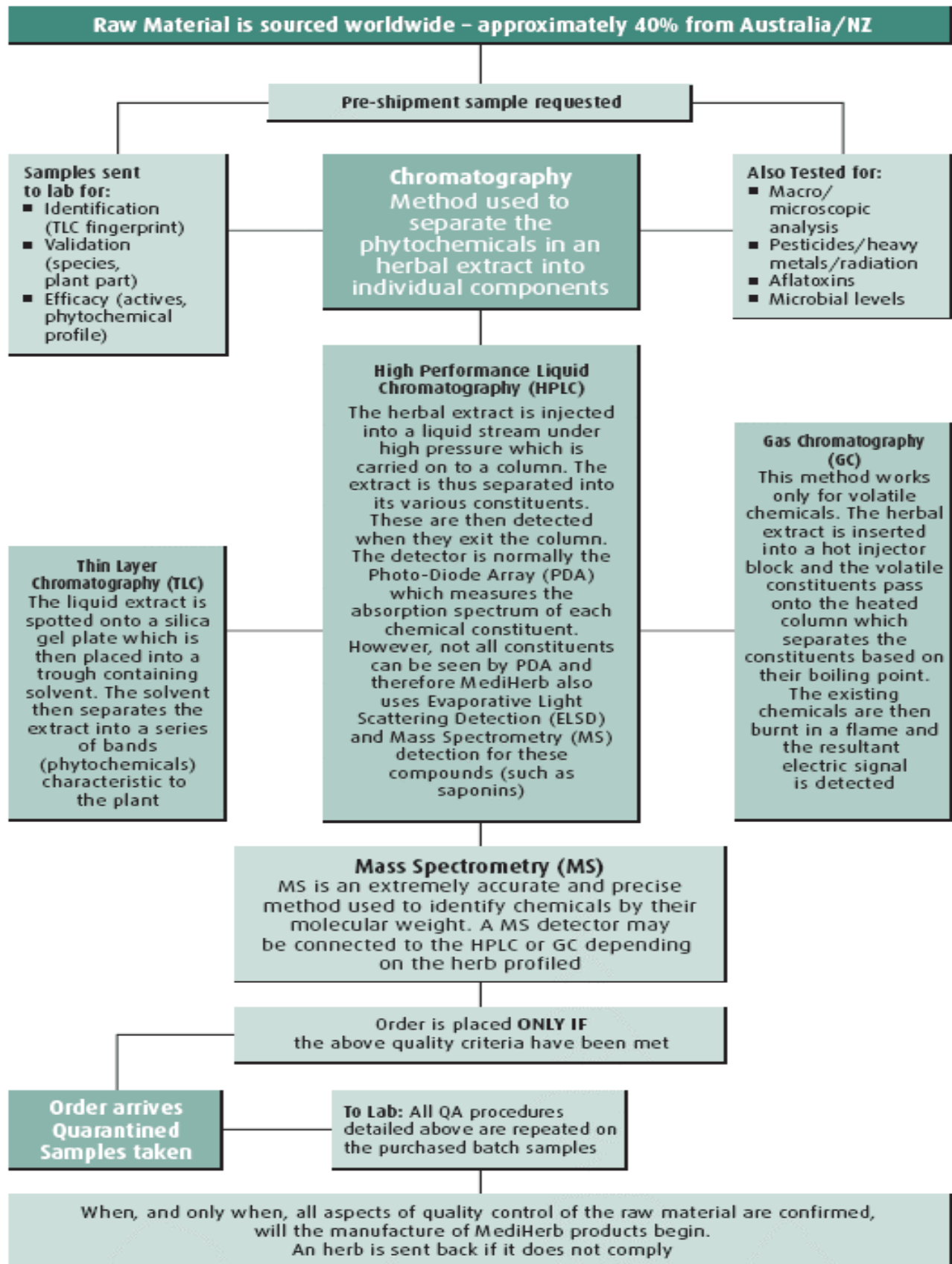
For further information on endangered medicinal plants visit:

[www.cites.org](http://www.cites.org)

[www.traffic.org](http://www.traffic.org)

[www.unitedplantsavers.org](http://www.unitedplantsavers.org)

# MediHerb Quality Assured Sourcing of Herbs



## Quality Assurance of Herbs (Identity and Purity)

Before any herb is purchased, a sample of the batch being offered for sale is analyzed by the Quality Control Laboratory and compared to the quality criteria specified by MediHerb. At this point, we regularly reject herbs as only the herbs that meet or exceed the strict quality criteria are purchased.

When we receive the purchased batch of herb, it is sampled according to a statistically valid sampling plan and then subjected to the same battery of tests as the pre-purchase sample. Only if the herb passes this second set of tests is the batch accepted into the factory for further processing.

Depending upon the specific herb, the quality assurance process includes testing herbs for:

- Color
- Aroma
- Texture
- Content of specified actives
- Thin Layer Chromatography fingerprinting
- Microbial levels
- Amount of extraneous matter
- Pesticides and herbicides
- Heavy metals
- Aflatoxins
- Radiation levels



Over the years, we have found many issues relating to quality, for example:

- Substitution of *Scutellaria lateriflora* (Skullcap) with other *Scutellaria* spp.
- Replacement of *Scutellaria lateriflora* (Skullcap) with *Teucrium* spp. (Germander)
- Adulteration of *Hydrastis canadensis* (Golden Seal)
- *Centella asiatica* (Gotu Kola) substituted for *Bacopa monnieri* (Bacopa)
- Substitution of *Stephania tetrandra* by *Aristolochia* spp., which has the potential to cause kidney failure
- Samples of *Andrographis paniculata* (Andrographis) upon testing at MediHerb, revealed to have no andrographolide content (the active constituent)
- Samples of *Vaccinium myrtillus* (Bilberry) upon testing at MediHerb, were found to contain a coloring agent, in order to imitate anthocyanins (the quality marker responsible for the blue color in ripe Bilberries). [Click Here](#) for Bilberry Adulteration Scientific Poster

Our stringent testing regimes guard against:

- **Substitution of species:** one herb may be substituted for another less costly herb
- **Adulteration of herbs:** a high quality and expensive herb may have a cheaper herb or pharmaceutical mixed in with it
- **Poor quality of herbs:** herbs can vary enormously in quality and this means the effect you and your patients feel can vary enormously

This ensures that the herbs approved for use in MediHerb products are of the correct species, are the correct plant part, have the correct active constituent profile and are free from contamination. Therefore you as the clinician can rest assured that the MediHerb product contains exactly what it says on the label.

## Substitution – Safety Considerations

Substitution of *Scutellaria lateriflora* (Skullcap) was a prominent issue in 2002 due to an Australian product being implicated in the death of a patient. The product contained Kava and two other herbs, one of these was meant to be Skullcap. However when the product was analyzed by the TGA (Australian equivalent of the FDA) it was found not to contain Skullcap. For this reason the TGA initiated a safety recall on this product and other Skullcap products from that same doctor-only company. In addition they also recalled other Skullcap products on the market. This is significant because substitution of Skullcap with the hepatotoxic herb Germander (*Teucrium* spp.) is well known and has been implicated in cases of liver damage in the literature. MediHerb became aware of this problem many years ago and established stringent quality procedures to ensure that our Skullcap products would always be authentic. In his capacity as a member of TMEC (Traditional Medicines Evaluation Committee) the forerunner of CMEC (Complementary Medicines Evaluation Committee), Kerry Bone alerted the TGA to the potential harm that could arise from this substitution. As a result the TGA took action in the 1990s to ensure that manufacturers only used authentic Skullcap. They conducted widespread testing of Skullcap products and found many products did not contain Skullcap as claimed. The fact that this substitution may have arisen again, particularly in the context of the case of liver damage, is cause for serious concern.



*Scutellaria lateriflora*

The substitution of *Stephania tetrandra* with *Aristolochia* spp. has been widespread in the herbal market with safety alerts being issued by the FDA, TGA (Australia) and MHRA (England). This followed the more than 70 cases of renal failure in Belgium associated with a weight-loss product that mistakenly contained a species of *Aristolochia* instead of *Stephania*. This inadvertent substitution is believed to have been due to the similarity of the Chinese common name: *Aristolochia fangchi* (Guang Fang Ji) and *Stephania tetrandra* (Fang Ji). *Stephania* is an important herb with good anti-inflammatory activity, linked to the bisbenzylisoquinoline alkaloid known as tetrandrine. MediHerb research evaluated by HPLC eight samples of herb labelled as *Stephania tetrandra*. Of these samples only one was believed to be *Stephania*; five samples contained aristolochic acids and were more likely to be *Aristolochia*; the remaining two samples contained neither aristolochic acids or tetrandrine, and were probably either *Clematis* spp. or *Akebia* spp. Based on this survey, the risk involved in the commercially available *Stephania* herb was evaluated as being too high to warrant its inclusion in the product line.

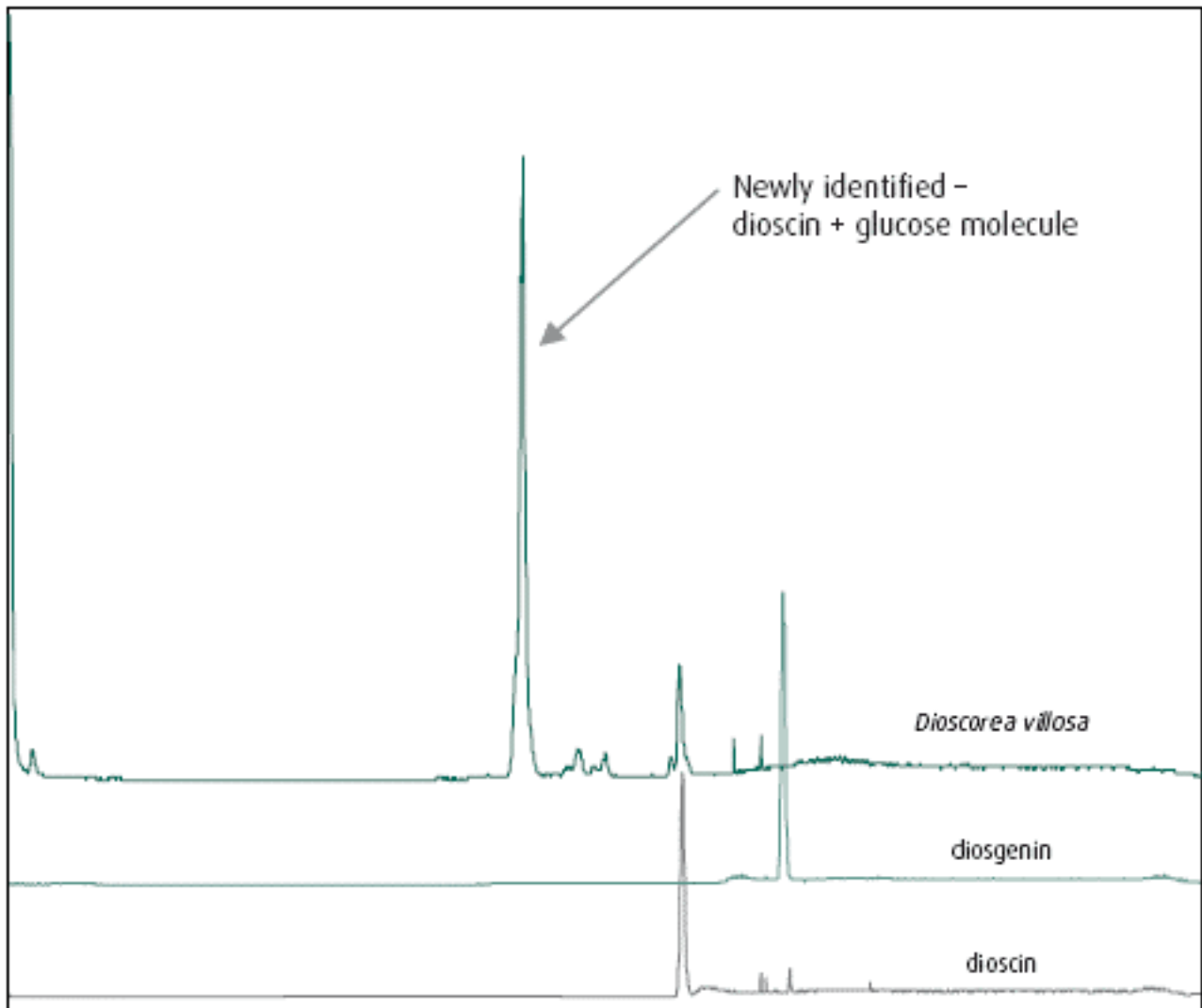
Our stringent testing regimes guard against substitution adulteration and poor quality

## Substitution – Efficacy

Through our research we have demonstrated that the alkylamide rich roots of *Echinacea angustifolia* and to a lesser extent *E. purpurea* have a modulatory effect on the immune system. However, when market surveillance was performed in October 2004 of eight American professional products of *Echinacea* tablets and capsules, only one was found to have appropriate levels of alkylamides but even then, the alkylamides were not of the most potent kind (2-ene). The name *Echinacea* is broadly used to describe all manner of preparations of the Purple Cone Flower plant: different plant parts and different species, but also different quality levels.

Commercial Wild Yam extracts available for use as raw materials are often not *Dioscorea villosa* but instead *Dioscorea opposita* (Chinese Yam Root) which has a different phytochemical profile and therefore a different clinical action. In addition to species substitution, it is widely misconstrued that *Dioscorea villosa* contains diosgenin and many products have this as a statement on their labels. However it does **not** contain diosgenin, but rather the diosgenin precursors. Traditionally *Dioscorea villosa* was believed to contain predominantly dioscin, however, the origin of this assignment is unclear (dioscin is a steroidal glycoside precursor of diosgenin). Research undertaken by MediHerb and Dr James De Voss from the University of

Queensland, Australia has found Wild Yam harvested traditionally contains only very small amounts of dioscin, not the predominance as previously thought. The major steroidal glycoside found was a diosgenin based compound that has an extra sugar molecule (either glucose or a similar sugar) to that of dioscin. Further research work continues. It is alarming that such a widely used herb is so misunderstood and substituted.



Cat's Claw (*Uncaria tomentosa*) has two chemotypes, the preferred chemotype contains only pentacyclic oxindole alkaloids (POAs) speciophylline, mitraphylline, pteropodine, isomitraphylline and isopteropodine; the other chemotype, contains the tetracyclic oxindole alkaloids (TOAs) rhynchophylline and isorhynchophylline in addition to the POAs. Traditionally only the POA chemotype was used therapeutically. This preference for the POA chemotype of Cat's Claw has been backed up by scientific research. MediHerb tests each batch of Cat's Claw to determine only the preferred POA chemotype is used to manufacture our Cat's Claw products.

Golden Seal (*Hydrastis canadensis*) is very expensive and has always been in short supply. As a result, substitution by other species is common. The herbs typically substituted are: *Coptis chinensis*, Indian Barberry (*Berberis aristata*), and Oregon Grape (*Berberis aquifolium*). These species do not contain hydrastine; they contain only berberine and berberine-related compounds. They do, however, produce an extract of



*Hydrastis canadensis*



the same color as Golden Seal. The berberine from Golden Seal and the herbs listed above is a potent antibacterial agent. However, it is the hydrastine that is believed responsible for the unique trophorestorative effects of Golden Seal upon mucous membranes. Similarly, the hair roots of Golden Seal, which have lower levels of hydrastine than the rhizome, are sold as the root and rhizome, which provides lower efficacy. The presence of hydrastine and the differentiation of adulterants is easily determined by HPLC. However, many companies do not have the necessary technology and often buy herbal ingredients without testing them. MediHerb only purchases cultivated Golden Seal, due to the report issued by CITES (Convention on International Trade in Endangered Species of Wild Fauna and Flora) that the herb is endangered in its native habitat. This is a very common example of

substitution of a less costly herb which greatly affects efficacy.

## Substitution – Cost

A very common case of substitution is with Tribulus due to the high cost of the raw material. Bulgarian clinical trials utilized a Tribulus extract characterized at 45% furanosterolic saponins by UV-Vis spectrometry, with the plant part being the above ground portion (leaves and stem). Many Chinese and Indian sources typically specify the fruit analyzed at 40% by gravimetry – not the accepted plant part nor analytical method. This discrepancy is easily overlooked and the price differential between the two extracts makes the genuine Bulgarian material economically unviable for many manufacturers. MediHerb has extensively investigated Tribulus and has presented a scientific poster on the comparison of the spectrophotometric and HPLC-ELSD analytical methods, highlighting the variability found in raw herbs of different origins. ([Click Here](#) to Download Tribulus Scientific Poster) It was shown that only by HPLC could an accurate quantification of the true constituents of the herb be performed. Herbal material from Bulgaria and Slovakia were the only sources found to have the same phytochemical profile as the clinically trialled extract. There was also a significant difference between the phytochemical profile of the fruit (part used in Asia) compared with the leaves and stems (clinical trials). Only the leaves and stems from Tribulus plants of Bulgaria or Slovakia contain any amount of the active marker compound, protodioscin.



*Tribulus terrestris*

## Storage and Handling of Herbs

After approval by the Quality Assurance process, all herbs are transferred to our refrigerated warehouse which is maintained at a constant 59°F and 40% humidity. Refrigerated storage, although expensive to maintain, avoids the need for any pesticides to be used for insect control. This ensures our organic herbs remain organic and ensures that all our herbs remain free of insect contamination prior to processing. Herbs are handled and processed at every stage with the utmost care. For example, herbs are milled in preparation for extraction under very low temperature cryogenic conditions to protect against excessive heating, which can damage the fragile active components.

## Quality of Extraction

MediHerb was co-founded by Kerry Bone, a first class honors graduate of Melbourne University who won the Masson Memorial Prize as Australia's top Chemistry student. After eight years as a research scientist, Kerry then completed, with distinction, the four-year Diploma in Phytotherapy from the world renowned School of Phytotherapy in England.

Upon returning to Australia to practice as an herbalist, he became frustrated with the poor quality of herbal extracts available at that time and the resulting effects for his patients. By applying his scientific training he developed a unique method of

extraction, termed 1:2 Cold Percolation. Word of these high quality herbal products spread and requests were soon received from health care professionals for supply around Australia and so MediHerb was born.

MediHerb is the first choice in herbal products for Australian health care professionals and since 2001 MediHerb has been available in the United States through our partnership with Standard Process Inc.<sup>®</sup> Both companies share the same philosophy and unwavering commitment to product quality and excellent service.

## Unique Extraction: 1:2 Cold Percolation Process

The 1:2 Cold Percolation method is unlike other herbal extraction processes; no heat or concentration are used, both of which may cause damage to the delicate plant material. The greatest care is taken to prevent any contamination from outside sources throughout the extraction process:

- All extraction equipment is designed and built from stainless steel
- Air used in the manufacturing complex is thoroughly cleansed using pharmaceutical standard filtering units

1:2 Cold Percolation, no heat or concentration  
therefore no damage to the herb's constituents

MediHerb prefers to use high quality dried herbs in making extracts rather than fresh herbs. Fresh herbs have a high water content, up to 80% and this makes for a weaker extract. In addition to the herb itself, we use only two other raw materials in manufacturing our herbal extracts, ethanol and purified water. Both are chosen very carefully to ensure the most efficacious product and meet pharmaceutical standard specifications.

All process water used in extraction is purified by reverse osmosis. First, it is filtered through numerous filter beds to remove particulate matter and organic compounds, then passed through reverse osmosis cartridges to remove the ionic materials before finally passing through an ultra-fine filter. The water produced is very low in all contaminants – organic, ionic and particulate – and is tested to comply with the *British Pharmacopoeia* specification for purified water BP2004.

MediHerb only uses ethanol that complies with the *British Pharmacopoeia* specification for ethanol, BP2004. Ethanol is essential to extract the full phytochemical profile of the plant, this cannot be achieved using water or glycerol alone. Ethanol has been used for hundreds of years in herbal extraction and old herbal texts discuss steeping herbs in wine over long periods. The human liver is naturally conditioned to metabolize small amounts of ethanol from ripe fruit and naturally fermented food. Any toxic effects from ethanol are dose-related and there is minimal risk of potential ethanol toxicity with herbal extracts due to the low daily dosage required. The usual recommended dose of most 1:2 herbal extracts is only 5 mL three times per day and in 5 mL there is approximately the same amount of ethanol as 1/6 of a standard glass of beer or wine.



*Silybum marianum*

Through our scientific analysis MediHerb has chosen specific ethanol percentages for each herb to maximize the quality, for example 25% ethanol extracts of Milk Thistle will not contain any silymarin because it is insoluble at this concentration.

# MediHerb Manufacturing Processes and Quality Control for Herbs

This Chart follows on from the Quality Assured Sourcing of Herbs Chart

## Cool room storage of herbs for quality assurance

Minimizes degradation of actives, control of insects, ideal storage condition for raw materials whose actives can degrade

## Raw material milled under cryogenic conditions so no heat can affect the phytochemicals

## Proprietary Cold Percolation

A unique slow process over 7-10 days known ONLY to MediHerb, developed by Kerry Bone, to extract the full spectrum of synergistic compounds of the herb without causing damage or degradation

## Liquid Extracts

The majority of our liquid extracts are made as 1:2 liquid extracts as this is the most effective method to extract the full phytochemical profile in a convenient dosage unit. However we also make 1:1 and 1:3 depending on the optimum extraction of the individual herb

Samples sent to the QA Laboratory where they are analyzed for phytochemical profile, level of actives, consistency, verification of original herb with no deterioration or degradation. This is the third round of testing performed. When the extract meets all criteria

Bottled for Sale



## Quality Guaranteed – The MediHerb "Quantified Activity" Program

The MediHerb Quantified Activity (QA) program aims to establish meaningful quality guidelines for the manufacture of herbal extracts. It is a system for ensuring the production of consistent quality extracts with guaranteed minimum levels of active constituents.

To date, MediHerb has quantified the activity of over 70 herbs through this program. To our knowledge such a program has never been undertaken in Australia, nor has it been matched anywhere in the world.

The constituents chosen as 'quality indicators' are carefully selected under the guidance of Kerry Bone and represent the most up-to-date scientific knowledge available.

The process of developing Quantified Activity extracts is complex and involves many steps. However, once the constituents are selected and the quantified activity levels are set, the main focus is to ensure the supply of consistent quality raw material and the retention of the constituents throughout the manufacturing process.

It is important to point out that Quantified Activity extracts are not purified single constituent extracts nor have they been manipulated in any way by non-traditional processes. They are whole galenical extracts of carefully selected whole herbs, manufactured using the MediHerb 1:2 Cold Percolation process, and still contain the complex range of active constituents from the raw herb. **In other words, quantified activity extracts are mainly achieved by the testing and selection of high quality, carefully dried raw materials.**



### The Echinacea QA Story

Echinacea is MediHerb's first quality story and a good example to explain the Quantified Activity program.

When MediHerb first started manufacturing in 1986 there was confusion in the global herbal industry over what constituted authentic Echinacea. *Echinacea angustifolia* and *E. purpurea* were routinely being substituted by unsuspecting manufacturers with another herb, *Parthenium integrifolium*. The substitution was made possible due to the uncanny physical similarity of the roots of Parthenium and especially *Echinacea purpurea*.

The solution implemented by MediHerb to guarantee supply of authentic Echinacea led to the development of the "Quantified Activity" program which exposed the Parthenium/Echinacea substitution and helped establish MediHerb's credibility in the herbal industry.

The earliest methods employed by MediHerb to assess herb quality and identity relied on a trained herbalist checking the herb's physical appearance, color, odor and taste. Taste was of particular importance because of the insight it gave into the herb's chemistry.



*Echinacea purpurea*

Traditionally, the test for Echinacea quality was the ability of the root to cause an intense tingling sensation in the mouth when chewed. The substitution of *Parthenium integrifolium* for Echinacea was successful only if appearance was checked and taste was not. When chewed, Parthenium root did not cause any tingling sensation in the mouth. The components which cause the tingling sensation from Echinacea are called alkylamides. So, one very simple solution was to taste the roots!

As MediHerb developed more sophisticated analyses, thin layer chromatography (TLC) was adopted which allowed the gross aspects of Echinacea's chemistry or its "chemical fingerprint" to be compared to a certified reference sample from the correct species. However, TLC mainly demonstrates if a compound is present, but not its quantity.

MediHerb understood that alkylamides were important for the efficacy of Echinacea and began to investigate methods to quantify the alkylamides along with other important compounds such as cichoric acid. At the time there was no published test methodology for alkylamides and the process of developing the high pressure liquid chromatography (HPLC) methodology took MediHerb a number of years.

Once armed with the HPLC methodology for identifying quality in terms of alkylamide content, MediHerb worked with Echinacea growers to determine appropriate growing conditions and handling parameters to ensure optimum retention of the alkylamides. Internally, MediHerb established protocols to ensure optimum retention and stability of alkylamides during all phases of the production process; from receipt of the raw material to completion of the finished product. Alkylamides are very delicate compounds and are easily damaged or lost during processing, hence developing these protocols took many years to conclude.

From these exacting analyses MediHerb was able to establish our standard for acceptance of Echinacea raw material based on alkylamide content. The task then was to work with herb growers to ensure that we were able to consistently source the herb according to our specification. Using our validated 1:2 Cold Percolation process we could then be confident that we would always extract a known amount of alkylamides along with all the other active compounds in every batch. Thus ensuring a consistent quality product with "Quantified Activity", every batch, every time.

The research into Echinacea continues today and our most recent efforts are aimed at further improving quality and efficacy, and understanding how Echinacea works. ([Click here](#) for further information on this ground-breaking research.)

## Quantified Activity and Standardization

At times, we receive an herb that has higher levels than our minimum specification, so you as the clinician receive that higher level of activity. We never dilute to meet a minimum specification. Herein lies the difference between Quantified Activity and standardization. With standardization, extracts with an active level that exceeds the specified standard would then be diluted to fall within that standard.

With the MediHerb Quantified Activity program, we have linked together all of the possible parameters that can affect product and extract quality and can guarantee that a high quality, efficacious extract will be produced every time.

## Standardized Extracts: A Balanced Perspective

In those cases where there are strong clinical data supporting the use of a particular standardized extract, MediHerb has adopted that standard and dosage approach for its tablet products. A good example is *Ginkgo biloba*.

There is considerable controversy and misinformation over the use of standardized extracts. Many of these are in fact full spectrum galenical extracts, made by traditional extraction with ethanol and water, which are merely produced to a consistent quality marker (or markers). No adulteration of the extract has taken place and isolated phytochemicals have not been added to the extract. Good examples of these are Devil's Claw, St John's Wort and Horsechestnut. In addition, MediHerb's extensive quality control procedures are capable of detecting adulterated or "spiked" extracts. Such extracts are never used in MediHerb products. For more information on this complex topic see Kerry Bone's articles (Modern Phytotherapist Vol 6, No [1](#) & [2](#)).



*Ginkgo biloba*

## Phytoequivalence

Phytoequivalence is a concept that was developed in Germany in the mid-1990s, and means that one herbal extract matches, or is equivalent to, another herbal extract, more specifically one of the clinically-proven extracts. It is somewhat of a misnomer as phytoequivalence really means chemical equivalence, ie that the two extracts have the same chemical profile. But it was also intended to mean more than that. Extracts that are phytoequivalent should be able to demonstrate the same pharmacological or physiological activity when ingested by humans. This is however difficult to demonstrate (for example, it could be done by showing the similarity of the levels of marker compounds (or their derivatives) in the bloodstream of humans after oral doses of the two products). A marker compound is a characteristic compound used to represent the quality standard for a standardized extract – it is often, but, not necessarily, one of the pharmacologically active compounds.

phytoequivalence = extracts that are physiologically equivalent

At the very least a match of the chemical profile, such as a chromatographic fingerprint, which outlines the full chemical spectrum of the extract is required. Comparison with the reference (clinically-proven) extract should indicate the presence of **all** major constituents, and the same levels of marker compounds and similar levels of **all** other measurable constituents. It is important to realize that phytoequivalence is **not** demonstrated by just comparing the level of only one or two marker compounds.

phytoequivalence = demonstrated similarity of all  
phytochemical constituents  
(all constituents present and at the right concentration)

Obtaining a good chromatographic fingerprint (usually by high performance liquid chromatography (HPLC)) for investigating phytoequivalence for an herb depends on several factors:

- A good extraction method to obtain almost all the pharmaceutically active compounds
- A chromatogram with good separation
- A representative concentration profile of the bioactive components detected by a proper detector

phytoequivalence = demonstrated similarity using  
appropriate methodology

Bulgarian clinical trials have shown that Tribulus leaf extract rich in protodioscin enhances libido and fertility and alleviates menopausal symptoms. If a Tribulus product is made from the root or fruit of the plant, or is sourced from anywhere else other than Eastern Europe, it will probably contain low levels of protodioscin and so will be quite different to the clinically-proven Bulgarian standardized extract. This is despite what might be claimed on the label for such products because often inferior methods of analysis have been used to measure the furostanol saponins (which includes the marker compound, protodioscin), such as gravimetric or colorimetric techniques. The phytoequivalence and quality of Tribulus products is best assessed by HPLC.



In a paper published in 2004, researchers from China compared 18 fingerprints of *Ginkgo biloba* extracts purchased from pharmaceutical stores, companies and collected from producing areas of China. All of these samples were supposed to meet the standard for flavonoids measured by ultraviolet spectroscopy. Standardized extract of Ginkgo from Europe was the clinically-proven extract used as the reference for phytoequivalence. The samples looked similar in the HPLC chromatograms, however further statistical analysis of this data indicated problems with three samples. A peak in two samples around the retention time of 10 minutes was much higher than the peak in the standardized Ginkgo extract, and was found to be the flavonoid rutin which had been added (in order to meet the old, UV spectroscopy standard). Inferior clinical results might well have been obtained using these non-phytoequivalent extracts.

MediHerb goes to great lengths using sophisticated analytical methodology to ensure that products such as Ginkgo 2:1 standardized liquid extract, Ginkgo 2000mg tablets, Tribulus tablets and Saligesic tablets are phytoequivalent to the clinically trialed products.

## Quality in Tableting "The MediHerb Way"

In recent times tablets have established a vital role in modern phytotherapy. Provided they retain the full potency of the galenicals, they represent a patient-friendly form of therapy which can vastly enhance compliance. Many experienced clinicians who are MediHerb customers rely on our tablet range for poorly-compliant patients and also to treat difficult or complex cases where just a liquid formulation may not be sufficient treatment on its own. In addition several herbs are best given in tablet form in order to conveniently achieve the necessary effective dose (as established in clinical trials eg Tribulus) or to avoid excessive amounts of ethanol (eg Boswellia).

We have a different way to make tablets – which is why we call it the MediHerb way. So what do we do that is different?

Firstly and perhaps most importantly, our unique cold percolation 1:2 liquid extracts are used in the manufacture of the MediHerb tablet range which means they are very potent and equivalent to the original galenical liquid extract. Many other herbal tablets/capsules are made from powdered dried herbs or poor quality dried extracts which means they are far less potent or potentially adulterated.

Secondly, our tablet production process has been the focus of extensive research and development to ensure that the finished tablet is as efficacious as the liquid extract, and that the full phytochemical profile has been retained.

From our research, we have found that the optimal method of herb processing involves the evaporation of the ethanol and water at low temperatures under vacuum. This important step minimizes the exposure of the delicate chemicals in the herbal matrix to the damaging effects of heat and oxidation.

The MediHerb tableting process takes this one step further to actually specify the optimal parameters employed during the evaporation and drying processes for each of the active constituents of the final tablet.

While the MediHerb cold percolation 1:2 liquid extracts are used for manufacturing our tablet range, there are on occasion some high quality extracts available from specialist extract manufacturers. In this case, we still apply the MediHerb stringent quality analysis at every step of the purchasing and manufacturing process to ensure our product is of superior quality. For example, there are many St John's Wort

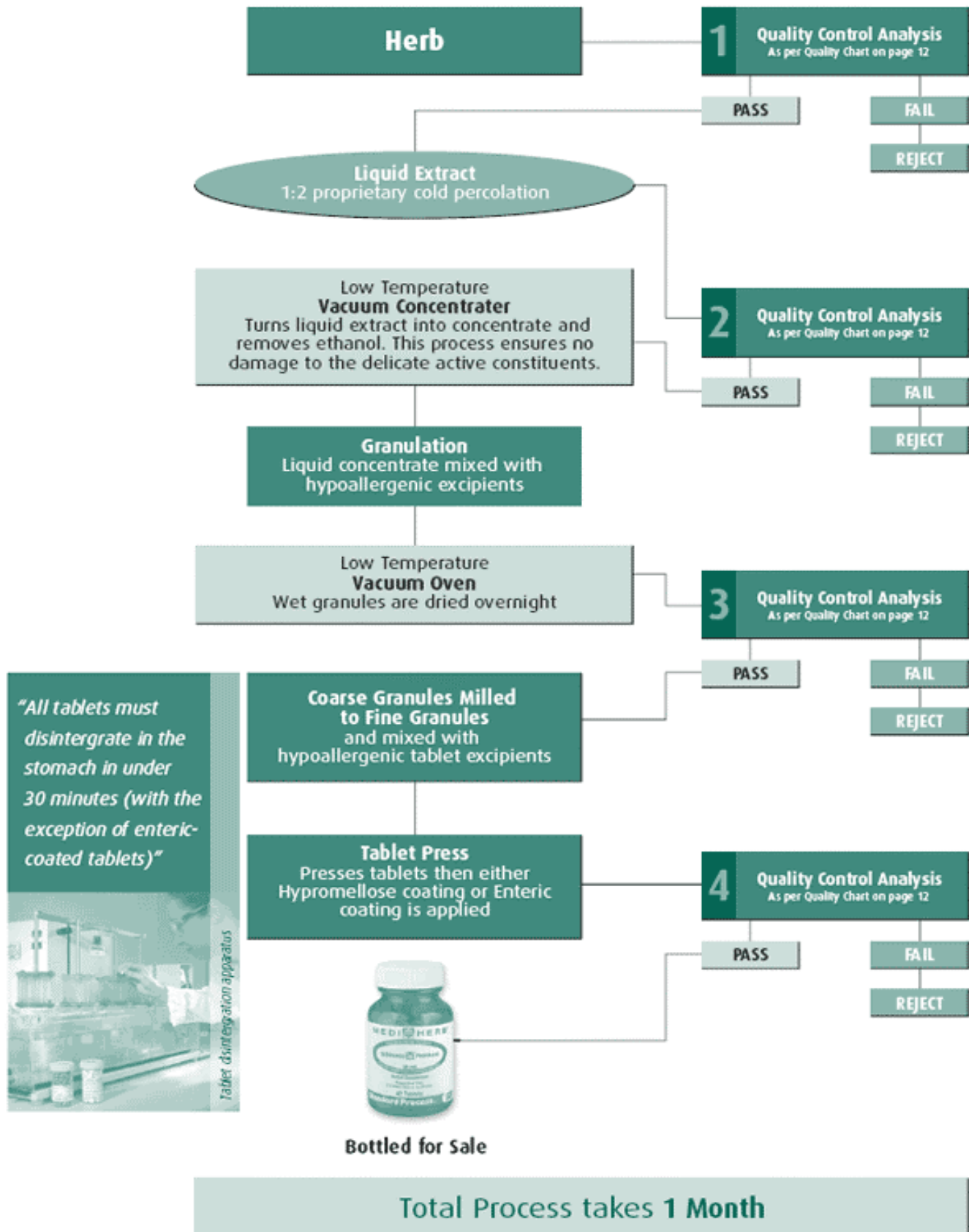


extracts available for purchase but of varying quality. MediHerb would only consider purchasing an extract if it exceeded our quality standards.

As with the MediHerb liquid herbal extracts, our tablets are manufactured to pharmaceutical standards. Each batch of tablets is tested for disintegration, friability, weight uniformity, and where relevant, for active constituents. However, it is only by ongoing research and control of all stages of the manufacturing process from **RAW HERB / EXTRACT > LIQUID > TABLET** that MediHerb has been able to produce superior tablet formulations, producing tablets with high active constituents that still comply to pharmaceutical standards.

MediHerb tablets must legally disintegrate in less than 30 minutes. This means that even patients with poor digestion can quickly and easily absorb our tablets for maximum efficacy. We believe that our tablets possess the equivalent bioavailability of liquids. The bioavailability of key constituents in our Echinacea Premium tablets has been verified in a clinical study.

# MediHerb's Unique Tableting Process Using Our Liquid Extracts



## Full Spectrum Extracts Mean Greater Efficacy but Lower Herb Equivalents per Tablet

Health care professionals often compare herb equivalence on tablet labels in an effort to gauge the most effective formula for their patients. However, herb equivalence can be quite misleading when comparing potency of products.

The process of standardization when misused can encourage an approach to manufacturing herbal extracts that only focuses on the one active constituent or marker compound while ignoring the remaining phytochemical profile of the herb. As we know herbs contain a wide variety of phytochemicals in an inert matrix of vegetable matter (eg cellulose). When an herb is extracted with a solvent, the resulting phytochemicals that are extracted will depend upon the type of solvent employed. Generally the insoluble matrix components will be left behind. By using a combination of solvents, one can very selectively extract an individual compound or one group of compounds. However this begs the question as to whether the process produces an herbal product or a product bordering on a pharmaceutical, because the phytochemical profile of the raw herb and the ratio of active constituents to marker compounds can be greatly altered.

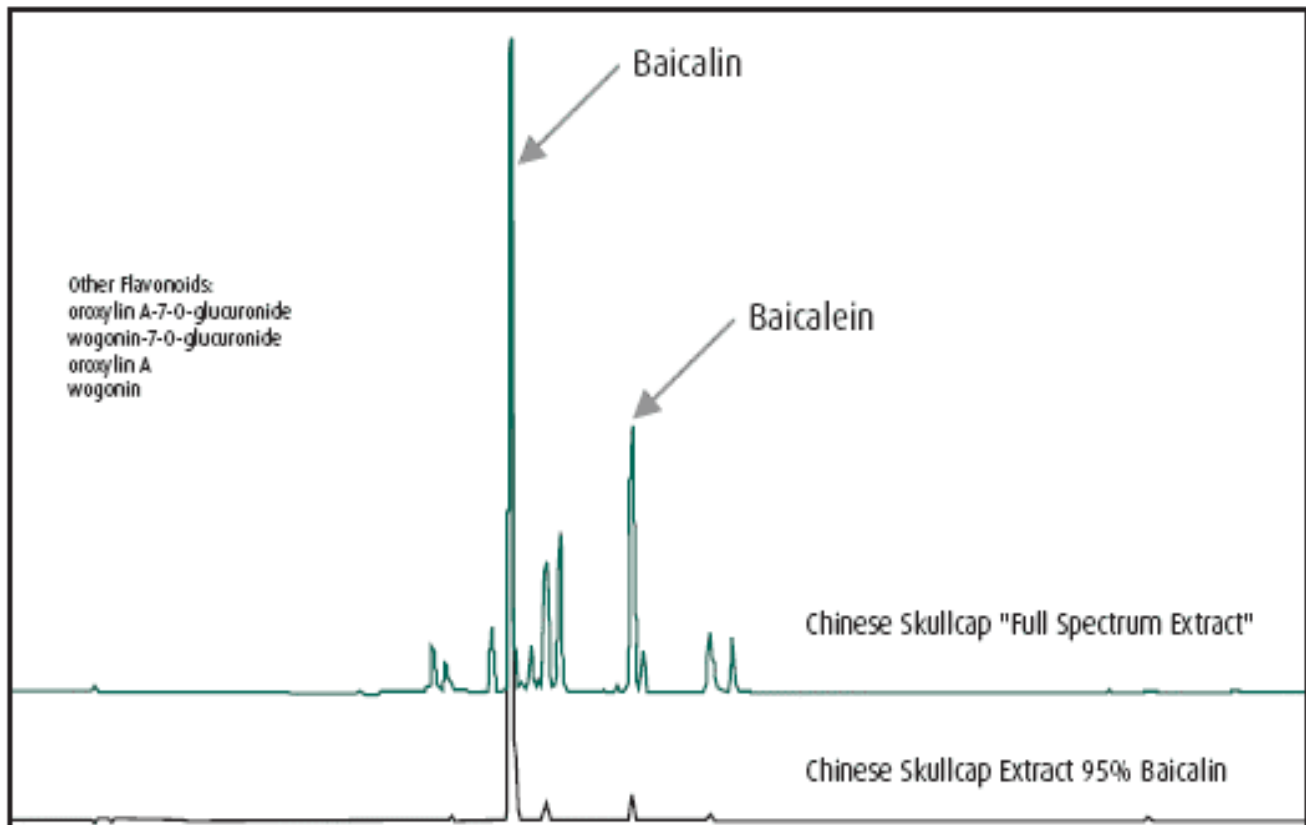


*Scutellaria baicalensis*

One example of this is the use of *Scutellaria baicalensis* (Chinese Skullcap) extracts, which only contain baicalin and do not contain any of the other 20 or more of its flavonoid constituents. These other constituents are typical of Chinese Skullcap, the most important of these being wogonin-7-O-glucuronide, oroxylin A-7-O-glucuronide, baicalein, wogonin and oroxylin A. Sources of Chinese Skullcap extract used in some herbal tablets contain greater than 95% baicalin, this means that less than 5% of the material is something other than baicalin. This is no longer an herbal extract and is rather a purified phytochemical (refer to the HPLC trace of Chinese Skullcap and baicalin below). These extracts are typically claimed to be a 20:1 dry extract and as such 500 mg of this extract placed into a tablet means the manufacturer or marketer of the product would be able to claim (20 x 500 mg) 10,000 mg of *Scutellaria baicalensis* dry root.

In contrast, the extract produced by extraction of Chinese Skullcap with 45% ethanol contains a very high level of solids material and a full complement of the many flavonoid components. As a result, a dry extract made from this liquid can only be manufactured with a 3:1 dry extract concentration factor. Adding 500 mg of this MediHerb extract into a tablet means we can only claim (3 x 500 mg) 1500 mg of *Scutellaria baicalensis* dry root.

## What was left out in these extracts to produce this product?



*This product would not pass the criteria set by MediHerb, as it does not contain the full phytochemical profile expected for Chinese Skullcap.*