

THE MEDICINAL PLANTS OPPORTUNITY

Entire contents © Copyright

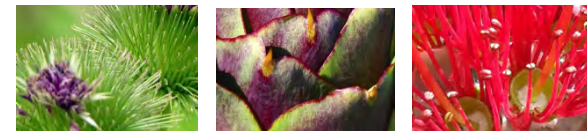
Phil Rasmussen

February 2022



Herbal medicine

- Herbal Medicine (Botanical medicine, Phytotherapy) the oldest form of medicine known to humankind
- Phytomedicines contain complex mixtures of phytochemicals.
- Natural functions of these include protectives against attack by predators, microbes & disease; C & N storage etc
- Approximately 25% of all drugs derived or developed from plants & their constituents



Egs of Drugs from plants

- Digoxin – from *Digitalis lanata*
- Morphine, codeine - from *Papaver somniferum* (opium poppy).
- Vincristine & vinblastine - from *Vinca rosea* (*Catharanthus roseus*, Madagascan periwinkle).
- Quinine, quinidine - from *Cinchona spp*



Some Challenges:

- Effective & safe?
- Chemical complexities, contain multiple phytochemicals.
- No single 'active constituent'.
- Often lack of research
- Huge diversity of products, delivery systems, strengths etc
- Regulatory – food or medicine?



Why herbal medicine?

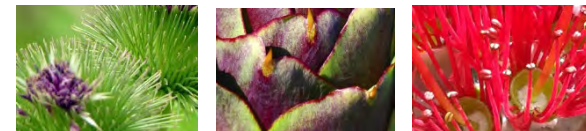
- Global demand for NHP's and in particular herbal medicines has been rising for many years due to a multitude of powerful market drivers.
- These include: aging populations; increasing costs of new drugs and hospital care; increasing evidence for the effectiveness of various interventions for a wide range of health conditions; increasing consumer appetites for natural wellness aids.
- Demand for various herbal medicines is exceeding supply.
- As with the global food supply chain, changing consumer preferences and climate change stressors are contributing to this supply shortfall.



Global opportunities

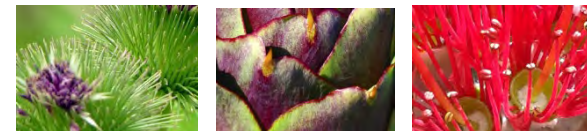
- 29 June 2011: OECD identified 5 ‘global shocks’ which will destabilise the world economy with increasing frequency in coming years:
- These were: Viral pandemics, cyber attacks, financial crises, socio-economic unrest & geomagnetic storms
- *A pandemic similar to the Sars outbreak in 2002 could spread quickly & with devastating effect “in Asia’s megacities”.*
- Antibiotic resistance & ‘superbugs’ becoming a major concern

Ref: NZ Herald, 29 June 2011



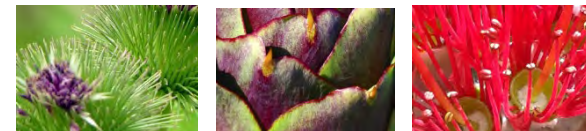
New Zealand's Strategic Advantages:

- Unique combination of geographical, soil & climatic attributes.
- High quality agricultural, biotechnological & medical science capabilities.
- Outstanding quality parameters of many medicinal plants grown here
- Encouraging results from fledgling growing & export-focussed operations
- Our 'clean & green' offshore image ideal for marketing natural health products offshore.



NZ Opportunities

- Increasing demands for high quality raw materials, and from cultivated rather than ‘wildcrafted’ sources.
- NZ has much potential to greatly increase exports of premium-priced, value added products (*L.E.K. Report on the NZ Natural Products Industry, May 2009*).
- Capacity to grow & produce natural health products whose bioactivity parameters rank them in the top end of the scale in terms of comparative quality with those produced elsewhere.



TIME magazine, Aug 18, 2003:

- Special edition, *'New Zealand Journeys - Cool Kiwis: Why its suddenly **HOT** on the edge of the world'*.
- Article about Biotechnology and bioprospecting of our natural resources, for future drug development.
- I argued that a bioprospecting model aimed at drug discovery is fundamentally the wrong objective.
- Compared to natural health products, drugs harder to discover & commercialise; also less downstream benefits to tangata whenua & Aotearoa.



Already a gamble, the work of bioprospectors is threatened by Maori claims to the country's natural treasures

By DANIEL WILLIAMS CHRISTCHURCH



ON THE FOURTH FLOOR of the chemistry building at the University of Canterbury, in Christchurch, is a freezer the size of a child's bedroom. Locked inside are some 10,000 samples of sea life collected off New Zealand or from neighboring waters during the past 20 years. Each creature has done its bit for science, having undergone a molecular strip search aimed at finding compounds that could be used to make new and better anti-cancer drugs. "We know jolly well the odds are against us," says Murray Munro, who with John Blunt heads the university's Marine Chemistry Group. But the possibilities draw the two sexagenarian professors into the lab each day to peer at extracts from the latest batch of specimens dropped off in jars and buckets.

In looking to the sea rather than the forests for answers to one of mankind's biggest killers, Blunt and Munro work in a new branch of what's called bioprospecting—searching nature for bioactive material that could be turned into something valuable, usually pharmaceuticals or herbal medicines. Like others around the world exploring the depths with the same goal, Blunt and Munro regard the sea as an untapped source of goodies.

Paradise for bioprospectors is any place teeming with life—and about 40% of all known species live in the sea. (Plants and fungi, which comprise roughly 20% of all living organisms, have yielded most of the life-

saving and pain-relieving drugs—quinine, penicillin, morphine—because until recently the bush was the only place researchers were looking.) All the better for bioprospectors, if an area supports an unusual mix of life—"because if you want to find novel compounds," says Munro, "you go to [places of] novel biodiversity." With a coastline stretching from sub-Antarctic to subtropical latitudes, New Zealand's waters are a bioactive smorgasbord, packed with the kinds of species that excite the pair most: sponges, tunicates (sea squirts) and bryozoans (sea mosses). It's likely that the cures for most diseases are in nature, waiting to be discovered. But the right of New Zealand organizations to look for them—no questions asked—is being challenged by indigenous groups.

These groups' ancestors were the country's first bioprospectors. Though there is some argument about this, Maori healers (*tohunga*) were probably using plants to make

TAG TEAM "What we've achieved together is far more than either of us could have done on our own," says Blunt, left, with Munro



medicines for centuries before British settlers began arriving in the late 1700s. Much of that old knowledge has been lost, and nowadays most Maori rely on western medicine. Even so, many object to researchers using nature for experiments in fields like bioprospecting and genetic modification. To these Maori, cutting open living things or mixing the genes of the same or different species "is analogous to . . . experiments on one's own family members," says Maui Solomon, counsel for three of the six tribes that lodged the ongoing Wai 262 claim, which reasserts Maori ownership of native flora and fauna. "While this may be regarded by some as emotional blackmail . . . the issue boils down to one of respect: respect for the fact that Maori have a special relationship with their natural world."

Though bold, Wai 262 has a legal basis. The Treaty of Waitangi, signed by chiefs and Queen Victoria in 1840, passed governance to the Queen but gave Maori "chieftainship over their lands, villages and all their treasures." That sweetener—open to interpretation—has gradually been eroded by subsequent legislation. The Continental Shelf Act 1964, for example, exerts Crown jurisdiction over precisely what Blunt and Munro are searching for: sedentary organisms on the sea floor.

Wai 262 isn't moving much faster than one of the professors' sponges. Lodged in 1991, it's become bogged down in the Waitangi Tribunal (a quasi-judicial body which investigates claims by Maori under the Treaty and makes recommendations to the Crown). But few observers are ruling out a pro-Maori verdict, which could cripple

New Zealand's bioprospecting industry were tribes to start demanding up-front payments for access to land or sea.

Such demands could be one consequence of a successful claim, says barrister Solomon. Another could be that Maori would become entitled to share in drug royalties. "But some are saying simply, 'Look, if you're wanting to mine our knowledge [of the natural world], then come to us, talk to us,'" Solomon says.

For now, Blunt and Munro press on. Thoughtful and urbane, they're not looking for a fight and point out that their work started more than 10 years before Wai 262 was filed. They don't get wet any more—that task falls to professional divers and some of the professors' students, who've done weekend scuba courses to extend their learning beyond the lab.

The professors focus on invertebrates because these are most likely to possess bioactive compounds. Way down in the evolutionary process, these creatures can't move and are often soft of body. So how do they defend themselves? "With chemical defense," says Blunt. "And if these chemicals are active against other living organisms, we try to tap into them, find out why and perhaps turn them to our advantage."

It's a numbers game. From 10,000 samples, Blunt and Munro have isolated more than 100 bioactive compounds, from which perhaps one—and they stress perhaps—will make it as a drug in the \$300 billion-a-year global pharmaceuticals market.

They have three compounds in pre-clinical trials with the Spanish drug company PharmaMar: one from a sponge plucked off the coast of Kaikoura, near the top of the South Island; one from a tunicate gathered further north; and another—the

one they're most hopeful about—from a sponge first picked up during a dive in Antarctic waters in 1989.

"A valuable bioprospecting discovery . . . can be worth many millions of dollars if it ends up contributing to a commercial product," says a recent New Zealand Government discussion paper. The government invests an estimated \$NZ5 million annually in the field, but most of it is going into the wrong kinds of bioprospecting, argues Phil Rasmussen, managing director of the Auckland-based Phytomed Medicinal Herbs. Lack of results so far—there's not a single drug in New Zealand's bioprospecting cabinet—has helped convince Rasmussen that bioprospecting aimed at drug development is "fundamentally the wrong objective" and that "some fairly serious [funding] mistakes have been made."

Even if a local group found the ultimate anti-cancer compound, New Zealand's small economy couldn't afford the colossal costs (\$200-500 million) of bringing it to market. And if you can't afford all the costs, you don't get all the benefits. The Madrid-based PharmaMar will be the big winner if one of Blunt and Munro's three promising compounds makes the grade. The professors say they couldn't have continued their work on public funding alone. "We do this [research] in an attempt to find out what is in our environment that could be of value to humans, to medical science," says Blunt. "But we also have to be pragmatic and say that in order to continue, we now have to have some tags."

What concerns Phytomed's Rasmussen is not just the surrendering of intellectual property to foreign companies, but the way research into herbal medicines suffers because of the government's preoccupation with drug development. Where marine bioprospecting is largely random, many of his company's remedies started as hunches inspired by traditional plant medicine (*rongoa Maori*). Well versed in Maori history and



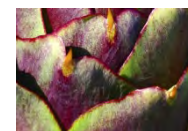
POTIONS—from commercial extracts like ginseng

sympathetic to bioprospecting, Phytomed cannot ensure the harvest of acceptable wai for New Zealand people if there is high-quality a result of bioprospecting. "That's our part," says Blunt. There's a field—not least guard to their amounts to an but not overly have guided a land chemist. Munro says, r therapy—and naturally occur span, perhaps Wai 262 doesn't enough to be Munro are going

SECRETS OF THE SEA

Phytomed Medicinal Herbs Ltd

- Incorporation of NZ native plants and organic herbs
- Adoption of sustainable business practices
- Validation of efficacy through clinical research
- Building a global, intrinsically New Zealand brand of herbal health products.
- Kiwiherb products aim to provide effective, safe & ethically-produced treatments or preventatives, to a wide range of common health conditions, particularly those for which current & future projected drug therapies are inadequate or less than ideal interventions.

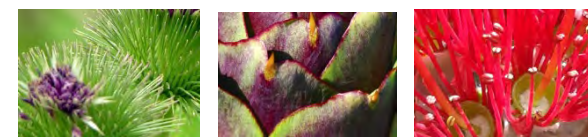
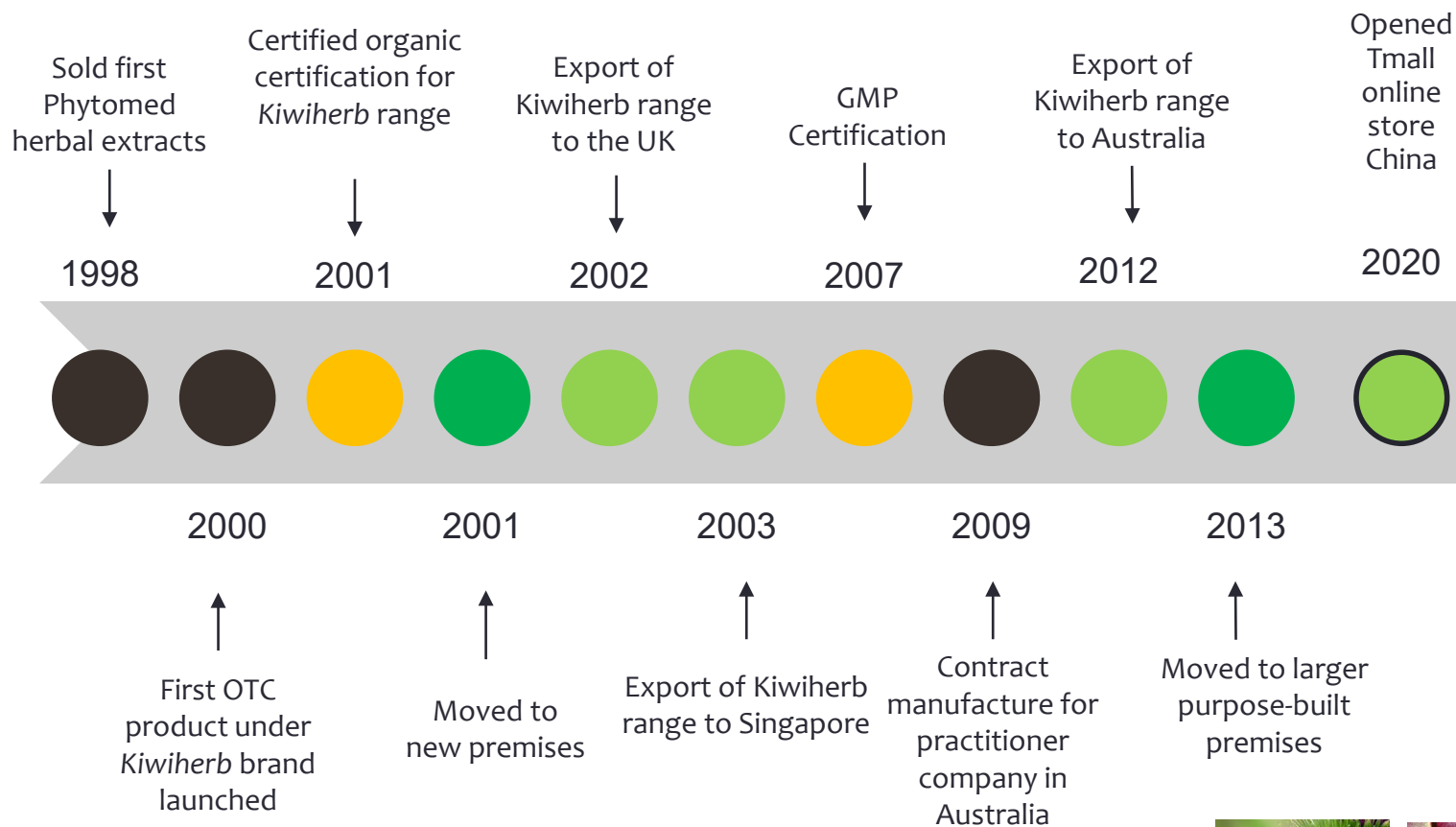








Phytomed Milestones



THE MANUFACTURING SUITE



2018



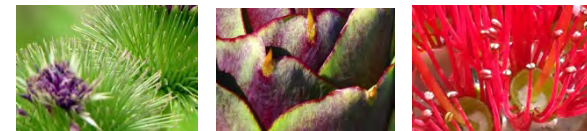
Stages of herbal quality

- Living plant
- Crude plant (usually dried herb)
- Extraction
- Formulation
- Stability



Determinants of Herb Quality

- Correct spp authentication, and variety or subspecies
- Source – country and conditions grown in
- Organic or not
- Harvesting methods
- Time of harvesting
- Post-harvest processing
- Age when purchased



Determinants of product quality

- Raw material quality
- Type of preparation (eg hydroethanolic liq extract, tablet, capsule, cream)
- Whether the wrong 'active' has been overly focussed on (eg hypericin; hyperforin; echinacea total phenolics)
- Manufacturing methods used
- Pharmaceutical parameters affecting bioavailability (eg excipients, particle sizes, tablet hardness etc)



Some Quality Acronyms

- GAP – Good Agricultural Practice
- GMP – Good Manufacturing Practice
- GLP – Good Laboratory Practice
- PV - Pharmacovigilance



Echinacea purpurea



Pharmacopoeial standards:

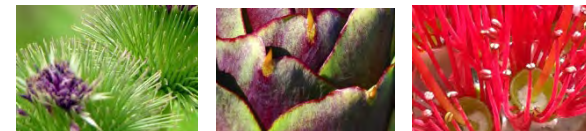
- European Pharmacopoeia
- British Pharmacopoeia
- British Herbal Pharmacopoeia (BHP)
- German Pharmacopoeia (DAB)
- ‘Herbal Drugs & Phytopharmaceuticals’, by M Wichtl (Medpharm) – 181 authoritative monographs.
- United States Pharmacopeia (USP) – increasing no of herbal monographs.
- Pharmacopeia of Peoples Republic of China; Japanese Pharmacopeia – Asian herb monographs.





Raw material tests

- Authentication of correct species & plant part undertaken
- European Pharmacopoeia (current edition) monographs used where available
- Methods include botanical characteristics (macroscopical & microscopical), organoleptic characteristics, comparison with validated reference specimens, chromatography
- Foreign material quantified (eg other plant material, soil etc); normal limit 2%
- Heavy metal tests for non-organic herbs
- Pesticide residues
- Microbial tests



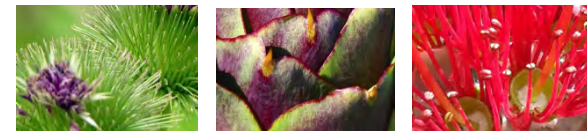
Certificate of Analysis:

- Identity confirmed.
- Country/location where grown specified
- Confirmation of correct organoleptic characteristics.
- Chromatography results
- Loss on drying within monograph limits.
- Heavy metals within monograph limits.
- Foreign matter within monograph limits.
- Miscellaneous tests for active or marker compounds.



Optimising consistency

- Use cultivated rather than wildcrafted herbs, from the same location
- Apply consistent and best practice post-harvest handling (*Good Agricultural & Collection Practice*)
- Apply consistent & controlled extraction processes
- Blend different batches to achieve consistent levels of actives



Goldenseal – alkaloid content of plant parts

	Hydrastine	Berberine
Standard	2% DW	2.5% DW
Leaf	0.80%	1.20%
Upper Stem	0.26%	1.08%
Lower stem	0.38%	1.45%
Rhizome	2.51%	4.52%
Root	1.57%	3.34%

Ref: NZ Institute for Crop & Food Research Ltd.



Some herbs being commercially grown in NZ

- Blackcurrant
- Comfrey
- Dandelion
- Echinacea
- Ginkgo
- Ginseng
- Globe Artichoke
- Green Tea
- Hops
- Lemon Balm
- Marshmallow
- Paeony
- Sage
- Valerian

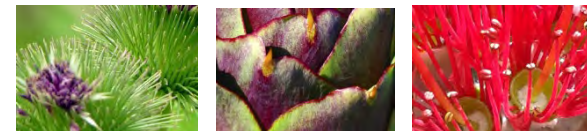


Hypericum perforatum (St John's Wort)



American Ginseng (*Panax quinquefolium*)

- Native of middle & northern states of U.S.A., parts of Canada, & extends to mountains far south, growing in rich soil and shaded situations.
- American ginseng (AG) history of medicinal applications developed by various North American Indian tribes.
- Similarities to Asian ginseng (*Panax ginseng*) recognised early on by Chinese, leading to AG being highly sought after in China as a substitute for this species.
- Many Chinese herbalists now using *Panax quinquefolium* as a substitute for the Asian species.







STANLEY

3

Life Guard

4

5

6

MADE IN U.S.A.

7

P.R. APPD
NO. 339 TG

8

9

THE STANLEY
WORKS © 1995

10

11

1F

12

13

14

15

3

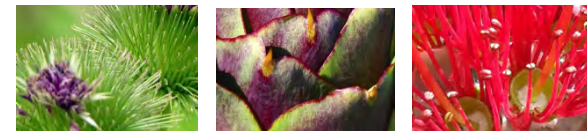
4

5

17

An endangered herb

- Gathering & export of large quantities to China occurred since 19th century.
- Wild sources have become rare, & AG now regarded as being at risk of extinction in the wild.
- Found in 34 states in US, 21 of which list it as a conservation concern.
- This due mainly to loss of habitat & over-harvesting
- Slow-growing and produces few seeds
- 1975: Listed in Appendix 2 of Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES).
- Cultivation increasing in Canada & U.S.



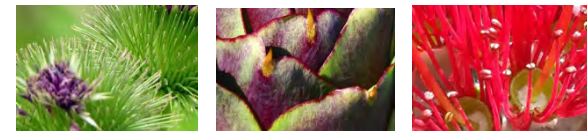
Pharmacology

- Adaptogenic
- Cognition enhancer
- Neuroprotective
- Antioxidant
- Cardioprotective
- Hepatoprotective
- Immunomodulatory
- Anti-cancer



Summary of Clinical Trials

- Useful adjunct in treatment of schizophrenia.
- Reduces fatigue in cancer patients, especially when still on chemotherapy
- Improves cardiovascular risk factors in patients with Diabetes Type 2.
- Prevention of upper respiratory tract infection in elderly.





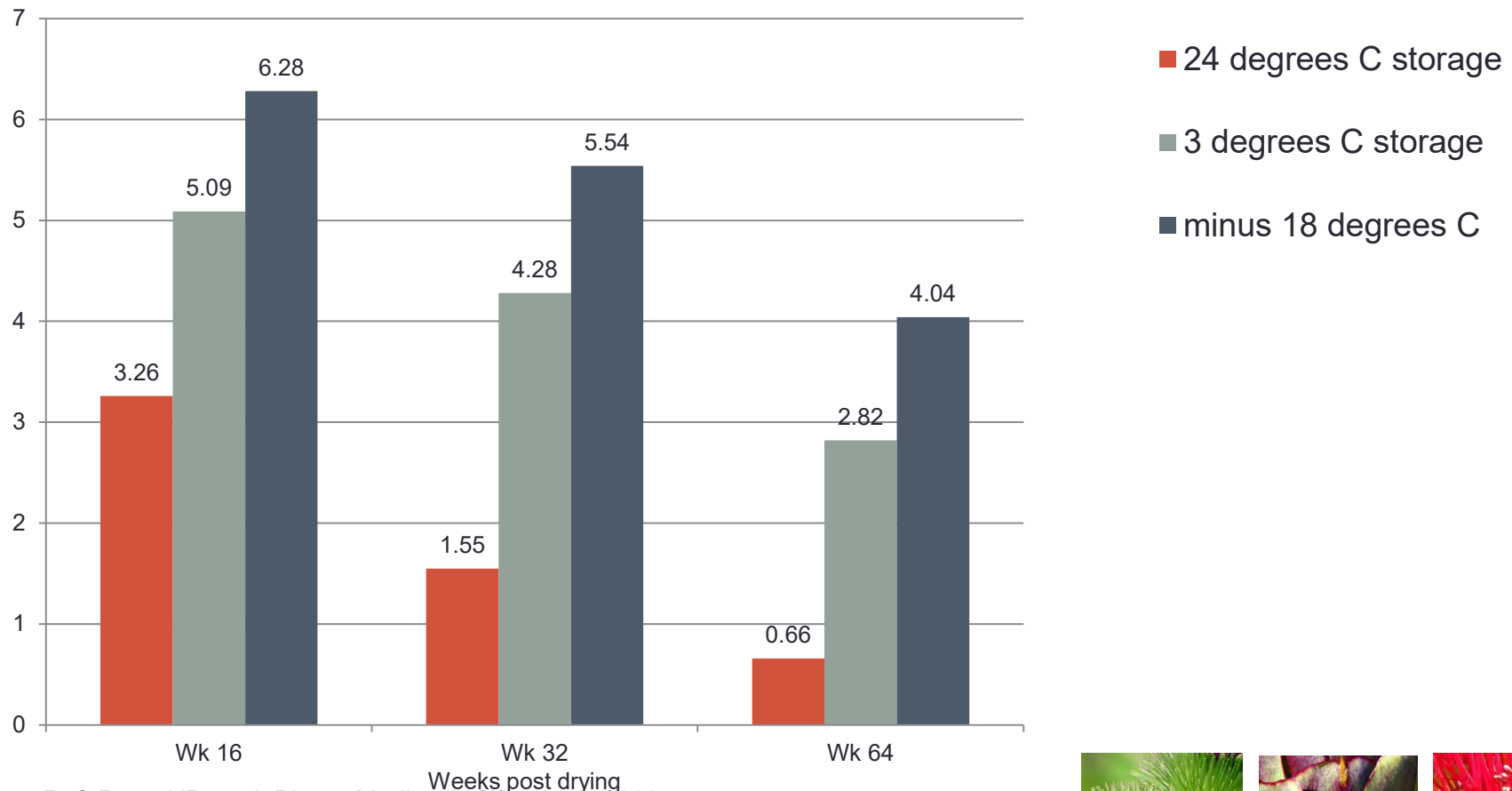
Echinacea spp (Purple coneflower)

- *Echinacea purpurea* – easier to grow organically, bigger root yields, & more published research than for *Echinacea angustifolia*.
- Root-based products traditionally used, for anti-inflammatory & immunomodulatory properties.
- *Echinacea purpurea* root shown to reduce prostate size in rats, & cause mice to live longer
- Most products in Europe made from flowering aerial pts, more likely to produce allergic reactions.

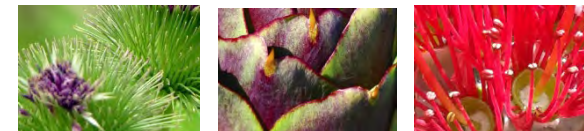


Echinacea purpurea alkylamides

- Alkylamide levels in mg/g dry weight upon storage



Ref: Perry NB et al, Planta Medica 66(1): 54-56, 2000.



Where to from here?

- Business model and Strategy!!
- What to grow?
- How much to grow?
- Harvesting & post-harvesting procedures?
- Where/how to sell?
- Capex & budget requirements
- Regulatory considerations



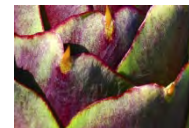
Sell to?

- Product manufacturers
- Farmers' markets
- Restaurants
- Specialty grocery stores; health food stores
- Brewers or distilleries
- Medical herbalists & naturopaths
- Herbal tea makers
- Own brand(s)?



Some Journals:

- BMC Complementary and Alternative Medicine
- Journal of Natural Products
- Journal of Ethnopharmacology
- Journal of Traditional Chinese Medicine
- American Journal of Chinese Medicine
- Phytotherapy Research
- Natural Product Research
- Phytomedicine
- Planta Medica



Other resources

- [Herbal Harvest](#), Commercial organic production of quality dried herbs. by Greg Whitten, Tasmania, Australia, Bloomings Books 2004
 - [www.herbblurb.com](#) – Phil's blog
 - [www.nutraingredients.com](#) – global trends & news
 - [www.naturalhealthproducts.nz](#) – national industry body
 - [www.nzamh.org.nz](#) – NZ Assoc of Medical Herbalists
- Phil Rasmussen: philr@Phytomed.co.nz
Mob: 027 2443116

