Speciality Non-food Crops

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Adrian P. Higson and Alison Hamer

Abstract Potential markets for non-food crops are both large and diverse, ranging from biofuels to performance chemicals and pharmaceuticals. If current consumer demand, high oil prices, and political support are maintained, we can expect to see significant increase in their cultivation. There are hundreds of crops in use or under development for non-food applications around the world. Speciality non-food crops are generally cultivated for specific natural products. They provide an invaluable source of therapeutic agents and high value ingredients including anti-oxidants and essential fatty acids for use in performance chemicals, cosmetics, functional foods, and pharmaceuticals. This chapter looks at the markets for renewable materials from speciality non-food crops and gives examples of crops currently under cultivation.

Current Status for Non-Food Crops

State of the Marketplace

The potential markets for non-food crops are both large and diverse, ranging from biofuels to performance chemicals and pharmaceuticals. Non-food crops are viewed as a means to improve industrial sustainability, improve rural economies and increase crop biodiversity. Globally, governments have developed a raft of policies and strategies to stimulate non-food crop markets and technologies (Alcimed, 2007; Defra and DTI, 2007; Hodsman et al., 2005; Schmitz, 2007; U.S. Department of Energy, 2006).

Comprised of five national bodies representing France, Germany, Netherlands, Belgium and the UK, the European Renewable Raw Materials Association (ERRMA) aims to promote the valorisation of compounds and materials derived from crops for use in the chemical and energy sectors. In the UK, significant progress has been made in the stimulation of markets; the number of farms growing non-food crops under schemes in England rose by 20% between 2003 and 2005. Many of the markets served by high value non-food crops are supply sensitive and can be prone to fluctuations in over and under-supply of material. There is interest and engagement from a widening range of players across the different sectors involved with non-food crops (Hodsman et al., 2005). However, engendering stable and profitable markets for novel crops is not without its challenges and barriers to uptake.

What is a Non-food Crop?

As the name suggests, a non-food crop is a crop used in applications other than for human food or animal feed i.e. the production of renewable

Adrian P. Higson (✉) and Alison Hamer
The National Non-Food Crops Centre, Biocentre, York Science Park, Innovation Way, Heslington, York, Y0105DG, UK
e-mail: a.higson@nnfcc.co.uk, a.hamer@nnfcc.co.uk

A.E. Osbourn and V. Lanzotti (eds.), *Plant-derived Natural Products*,
DOI 10.1007/978-0-387-85498-4_25, © Springer Science+Business Media, LLC 2009

energy, fuels and materials. It is the intended application, or use, that denotes their status, and therefore they are not necessarily distinct from traditional food or feed crops.

From amaranth and artemisia to yarrow and yew, there are hundreds of crops in use or under development for non-food applications around the world. The UK's National Non-Food Crops Centre (NNFCC) holds agronomy and market details on about a hundred of the key European crops.

The majority of non-food crops also have food and/or feed uses, for example wheat and oilseed rape (OSR). The use of existing food crops with well-understood agronomy and developed supply chains can offer an easier route to market over the development of completely novel non-food crops. Current crops dominating the non-food area are those that produce sugar, starch and oils, for use in the production of fuel and bulk chemicals.

Three groups of crops grown solely for industrial, or non-food, purposes are; fibre crops, energy crops and crops grown for their secondary metabolites. In addition to their well-known historical uses, fibre crops such as hemp and flax are used in biocomposites for the automobile industry and in construction materials. Increasingly, crops such as miscanthus and short rotation coppice (SRC) willow or poplar are being cultivated for energy production. Energy crops are grown to maximise yield of biomass per hectare, and developments in the thermal processing of biomass (Bridgewater, 2006) or the manipulation of carbohydrates like starch and cellulose could result in these crops forming the basis of a new economy based on renewable resources ('the bioeconomy') (Morris, 2006). The third type of non-food crop is the low volume, speciality crops grown for components such as secondary metabolites or specific oils. Often with long histories of wild harvesting for traditional use, they are grown to provide plant-derived pharmaceuticals and speciality chemicals for use as personal care and functional food ingredients. Although not always high value, in general, the profit margins available in these high value sectors make the business risk of developing novel non-food crops acceptable. This review looks at activity in the area of speciality non-food crops with respect to secondary metabolites and speciality oils, crops for fibres such as jute and cotton are not considered. Although not strictly 'non-food', crops used to produce ingredients for functional foods have been included as the areas of healthcare and nutrition are closely related, and the movement of functional food ingredients (e.g. omega oils) into personal care products is also evident.

Although a large amount of data is available for large volume crop cultivation, information on the cultivation of speciality crops is less available. The situation is further complicated by the dual use of crops in food and non-food applications. Table 1 serves to give an idea of the cultivation levels of a range of speciality non-food crops in Europe. For comparison, approximately 5 and 25 million hectares (ha) of European land (EU27) are used for OSR and wheat cultivation annually. Land used for cultivation of crops for herbal remedies in Europe amounts to 70,000–100,000 ha (Williamson and MacTavish, 2007).

Table 1 European non-food crop activity (2004) (The Promotion of Non-Food Crops; Hodsman et al., 2005)

Crop	Country	Area (ha)
Caraway	Lithuania	6,500
Chamomile	UK	175
Crambe	UK	1,171
Lavender	France	24,000
Linseed*	Finland, France, Germany, Lithuania, Poland	>7,465
Poppy	France, UK	8,466
St John's Wort	Austria	24
Sunflower	Austria, France, Germany	71,503

* Area not available for all countries

History of Non-food Crops

It is said that "there is nothing new under the sun" and certainly the use of plant products for their functional properties in the home and garden is as old as man himself. Plants have been used for home building, to produce heat, provide decoration and to treat diseases. The first agricultural (Neolithic) revolution some 10,000–12,000 years ago changed man from a nomadic hunter-gatherer to a settled cultivator of crops. The growing of herbs for culinary and medicinal purposes can be traced to ancient Egypt and Mesopotamia. These gardens later appeared as the physic gardens (e.g. Chelsea Physic Garden), of the sixteenth and seventeenth centuries.

Throughout the seventeenth and eighteenth centuries, the understanding of herbal medicines increased to a point in the mid-nineteenth century, where chemists were able to characterise the principle active ingredients in a number of medicines (Fowler, 2006; Sneden, 2005). These active ingredients, included morphine (from *Papaver somniferum*), digitalis (from *Digitalis purpurea*) and quinine (from *Cinchona* tree bark), and provided the impetus for experiments which changed the direction of medicine and gave rise to the chemicals industry. Throughout history, chemicals have been isolated from plants; written records for the use of indigo exists from Mesopotamia (seventh century BC) and by 715 BC wool dying was an established craft in Rome. In the 1850s the paths of herbal medicines and dyes crossed, changing the future development of both products. In 1856, the English chemist William Henry Perkin set out to chemically synthesise the natural product quinine from aniline. Quinine, an expensive plant extract was in demand at the time for the treatment of malaria. Rather than obtain quinine, Perkin synthesised the deep magenta dye '*mauvein*'. This serendipitous discovery paved the way for the modern dyes industry. It also laid the foundations for industrial organic chemistry which would go on to play the fundamental role in shifting western medicine from plant-based herbal extracts to synthetic single entity drugs.

By 1900, purified plant drugs were in use, from these purified compounds came new semi-synthetic drugs and by the 1950s plant compounds were being regarded as starting points for drug development rather than final compounds. From the 1950s fully synthetic drugs (although based on natural product leads) became the preferred route to therapeutic agents. Despite the twenty-first century preference for synthetic drug production, the plant kingdom still provides us with important drug starting materials, and active ingredients competitive with or beyond the commercial reach of synthetic chemistry (Table 2) (Butler, 2005; Ganesan, 2004).

Table 2 Examples of medicinal drugs derived from plants

Crop	Active ingredient	Therapeutic area	Chemical family
Artemisia annua	Artemisinin	Anti-malarial	Sesquiterpene lactone
Catharanthus roseus	Vincristine, vinblastine	Cancer chemotherapy	Bis-indole alkaloids
Cinchona ledgeriana	Quinine	Anti-malarial	Quinoline alkaloid
Digitalis purpurea	Digoxin	Heart conditions	Steroidal glycoside
Narcissus pseudonarcissus	Galanthamine	Alzheimers disease	Isoquinoline alkaloid
Papaver somniferum	Codeine, morphine	Analgesic	Opiate alkaloids
Pilocarpus jaborondi	Pilocarpine	Glaucoma	Imidazole alkaloid
Taxus genus	Paclitaxel	Cancer chemotherapy	Diterpene

With the advent of synthetic chemistry, interest in non-food crops waned somewhat. The sector was affected by the availability of cheap oil, resulting in petrochemicals forming the basis of our manufacturing industry. However, as the twenty-first century develops, we see a reawakening of interest in their cultivation. The reasons for the uptake of plant-based materials differ from sector to sector, but in general focus on: mitigation of climate change; security of energy supply; high oil prices; amelioration of environmental contamination; consumer demand for natural ingredients and improved material performance.

While some sectors (e.g. natural dyes) show little sign of recovery, others (e.g. plant-derived fuels named biofuels) are being driven by government incentives and progressed through advances in technology. Other sectors such as plant-derived pharmaceuticals, personal care products, lubricants, and other chemicals are developing based on consumer demand, technical innovation, regulation, and favourable economics.

Crop and Product Development

Overcoming Complexities, Challenges and Opportunities

As with all products, the introduction of new materials from crops requires the development of new supply chains. These supply lines originate at the agricultural/horticultural industry and are often unfamiliar to companies who traditionally work with petrochemical-based feedstocks. Companies will often need to develop new skills and technologies or seek out partner companies to ensure supply chain competency and security. The following areas need to be understood and considered when developing new plant-derived products:

- Knowledge of plants and bioactive contents
- Ability to source sustainable plant material (germplasm)
- Plant breeding, cultivar optimisation
- Agronomy, agricultural scale up, traceability, Good Agricultural Practice (GAP)
- Effects of genotype and phenotype on yield of natural product
- Post-harvest storage, initial extraction
- Separation, purification, standardisation, characterisation
- Synthetic derivatisation
- Regulatory framework; safety, efficacy, clinical trials
- Market demand and acceptance
- Co-ordination of multidisciplinary projects
- Understanding and financial support from private and public sectors

The cultivation of non-food crops can be integrated into the supply chain through a number of routes. Low volume crops can be cultivated by the final product supplier. This production route provides the maximum control over the quality and consistency of cultivation. This control is particularly important when the end product is a botanical extract containing multiple constituents and for use in pharmaceutical applications. The end product manufacturer can contract cultivation to a third party; this approach is often preferable for companies not focused on plant breeding or agronomy. The third supply route is to purchase material from agricultural contractors who have detailed knowledge of agricultural markets and existing supply chains. This route is more common for larger scale production of food crops and crops for biofuels, but is also well demonstrated by plant oil supply chains. For example, in the UK, contracts are available to farmers for borage, echium, and camelina, details of such contracts are held by The National Non-Food Crops Centre.

The complexity of supply chains and the need to develop collaborations is seen in the cultivation of sweet gale (*Myrica gale*) for use as a cosmetic ingredient (Galley and Simpson, 2007). The deciduous shrub sweet gale (also known as bog myrtle or Dutch myrtle) has been used for flavouring beer, as an insect repellent and an herbal remedy. More recent analysis showed extracts displayed interesting anti-bacterial activity against acne-causing skin bacteria. Although harvested from the wild for thousands of years, sweet gale had never been commercially propagated or cultivated. To develop cosmetic products containing sweet gale, a consortium capable of the following was required; identifying the best plant material, developing the propagation and agronomy, designing bespoke harvesting machinery, developing bioactive extraction processes, and performing product formulation and safety tests.

Analysis of wild sweet gale showed considerable variation in composition from plant to plant and also by location. The Scottish Agricultural College (SAC) developed tests allowing standardisation of extracts and developed propagation methods. SAC also developed an understanding of the agronomic requirements for commercial production. Highland Natural Products Ltd. performed environmental impacts assessments on commercial production and looked at economic effects of land use. Two critical technologies needed to be developed. Cranfield University (UK) designed and built a harvester suitable for the wet upland conditions. Critical Processes Ltd. assessed extraction methods and optimised a steam distillation process. Product formulation, efficacy, and safety tests were performed by Boots. The development project resulted in new products forming part of the Boots 'Botanics' range. Sweet gale oil is the first essential oil to be developed in 40 years and plans to cultivate 5,000 ha are underway.

Development of New Crop Varieties

Developments in high-throughput screening technologies now allow the rapid and detailed analysis of genes, transcripts, proteins and metabolites. Studied in combination, 'systems biology' creates new opportunities for both conventional development of new crop varieties and transgenic modification (or genetic modification, GM) (Miflin, 2000; Smallwood, 2006). This understanding can be used to improve both input (inputs required for successful cultivation, e.g. water, fertiliser, fungicides and pesticides) and output (quality and quantity of the desired products) traits in food and non-food crops. Although resistance to the cultivation of GM crops in Europe is strong, it has been estimated that worldwide, GM crops cover almost 4% of total arable land (WHO, 2005). GM strains of maize, soybeans, OSR and cotton are grown commercially. Also, GM papaya, potato, rice, squash, sugar beet and tomato are available. In the EU, GM 'Bt maize' – a variety containing a gene that allows the maize to defend itself against the European corn borer – was grown on more than 100,000 ha (250,000 acres) in 2007 (EuropaBio, 2007). Currently focused on agronomic trait developments which minimise economic damage in crops, such as increasing pest or disease resistance, pesticide tolerance and crop yield, the potential exists through metabolic engineering to optimise the production of specific fatty acids and secondary metabolites in crops (Kinney, 2006; Smallwood, 2006). An active area of research and development is in the production of biological therapeutic compounds (biologics) in plants and is discussed further in Section 3.2.

Biorefineries

Biorefineries are large integrated facilities, which, by 'biorefining', provide a range of products including fuel, chemicals, and power from bio-based feedstocks. Key to the successful development of biorefineries is the availability of technologies to derive maximum value from all constituents of a very high volume of biomass, thus it is not currently clear to what degree they will drive market uptake of speciality crops. Driven by a high volume chemical or biofuel, the co-processing of extraction products such as waxes, terpenes, proteins, sterols and antioxidants plus the efficient use of other polymers such as lignin for heat and power generation or chemical production will be required to derive maximum economic returns (Tamutech Consultancy, 2007). Through the operation of biorefineries, even materials that are present in low concentrations may become commercially viable.

There is a very wide range of potentially valuable extracts from plant biomass. Many of these are specific to particular genera or species. Others are found quite widely across the plant kingdom. Ingredients from a specific type of plant, e.g. a natural product pharmaceutical ingredient, will normally be extracted in a dedicated facility, which is unlikely to form part of a biorefinery. However, more generic materials found in many types of plant; particularly crops associated with biofuel feedstocks e.g. maize, wheat and OSR could be extracted.

The extraction of squalene is a notable example of a terpene found in low concentration in a range of plants. It is normally produced from shark liver oil, but during the process of refining low grade olive oil, squalene is concentrated in a fraction called the deodorizer distillate. Ten percent or more of this fraction can consist of squalene, and extraction becomes cost-effective. The squalene is hydrogenated to give squalane, a high value ingredient in demand for cosmetic and personal care products (Bondioli et al., 1993; Fernández-Bolaños et al., 2006).

Non-food Sectors

Pharmaceuticals

Natural products and their derivatives are an invaluable source not only of lead compounds for pharmaceutical development but also therapeutic agents themselves (Table 2) (Fowler, 2006). In terms of production cost, the chemical complexity of these agents places them beyond the reach of synthetic chemistry and natural product extraction, and derivatisation is the preferred production route (Butler, 2005; Fowler and Law, 2006; Koehn and Carter, 2005; Srivastava et al., 2005). This approach is exemplified by the manufacture of the taxanes, paclitaxel and docetaxel. These compounds form the basis of the blockbuster drugs Taxol® and Taxotere® which are used to treat many types of cancer. Taken from yew species (*Taxus* spp.) both natural paclitaxel and synthetic intermediates suitable for conversion to paclitaxel and docetaxel are extracted.

First performed in 1804, the extraction of morphine from opium poppies (*Papaver somniferum*) still provides an important source of opiate analgesics and a starting material for codeine synthesis. These alkaloids are widely used in the treatment of severe pain. As for the taxanes mentioned above, extraction from the poppy remains the preferred route for the production of morphine and codeine. Globally, opium poppies are legally cultivated on around 40,000 ha annually. The major supplier of opium poppies is Tasmania, supplying around 40% of the market. GlaxoSmithKline, Tasmanian Alkaloids and Johnson-Matthey operate fully integrated supply chains for opiate production. Levels of production are controlled by the UN Single Convention on Narcotic Drugs, which limits production to reasonable saleable quantities with allowance made for contingency stocks (Fowler and Law, 2006).

Plants are an important source of new drug leads (Fowler, 2006; Kong et al., 2003). Developments continue across a number of scientific areas (e.g. plant molecular biology, extraction and separation technology and molecular characterisation tools). Plus, there is increasing concern about the lack of new pharmaceuticals entering the marketplace. Therefore, interest in the cultivation of high value non-food crops for pharmaceutical applications is re-emerging. The reasons for this renewed interest have been reviewed in detail (Fowler and Law, 2006) and are summarised below:

- Lack of delivery at the expected levels of synthetic and combinatorial chemistry.
- Recognition that natural product-derived drugs occupy a very different 'chemical space' to synthetically derived drugs, providing an important extra dimension of chemical diversity - this is especially true of plant systems.
- Significant advances have been made in technologies for preparation of plant extracts and the identification and rapid isolation of specific active entities (de-replication).

A number of companies hold valuable libraries of natural products (Fowler and Law, 2006). Phytopharm Plc and GW Pharmaceuticals Plc are developing new drug pipelines based on medicinal plants. In collaboration with Unilever, Phytopharm are developing a functional food targeted at obesity sufferers. The extract from the South African *Hoodia* plant, is claimed to contain a novel satiety stimulator that reduces calorie intake in overweight subjects. In addition to detailed agronomy studies, Phytopharm are developing supply chains and undertaking clinical and consumer studies.

Cannabis (*Cannabis sativa*) has a long history of medicinal and non-medicinal use and records date back 4,000 years. Naturally occurring cannabis contains a unique class of compounds known as cannabinoids. Over 60 members of this family have been identified but only a few have been well studied. The two best known and most studied cannabinoids are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) (Fig. 1). These two compounds show markedly different pharmacological activity. THC is best known for its psycho-activity but also displays analgesic, anti-spasmodic, anti-tremor, anti-inflammatory, and anti-emetic activity. CBD

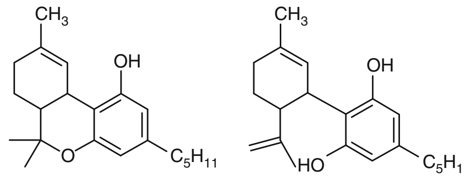

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Fig. 1 Cannabinoids delta-9-tetrahydrocannabinol (1) and cannabidiol (2)

has anti-inflammatory, anti-convulsant, and anti-psychotic activity as well as neuroprotective and immunomodulatory effects. Critically, CBD is not psychoactive or intoxicating and may play a role in reducing the unwanted side effects of THC.

GW Pharmaceuticals are leading research into the use of cannabinoids for treatment of a range of illnesses such as Multiple Sclerosis symptoms including muscle spasticity, spasms, bladder dysfunction and pain control. The company states that precise pharmacological activity can be achieved by blending different cannabinoids in defined ratios. In addition to the ratio of cannabinoids; GW are interested in the action of other plant components modulating pharmacological activity.

By its nature, the cultivation of *Cannabis sativa* plants requires additional control beyond Good Agricultural Practice (GAP) and Good Manufacturing Practice (GMP) requirements for plant-derived pharmaceutical production. GW cultivates *Cannabis sativa* under licence from the UK Home Office and the crop is grown under a highly secure and controlled glasshouse environment. Computer control allows temperature, humidity, air change, and photoperiod to be optimised to give a controlled year round supply of material. Initial crops were grown from seed but subsequent chemovars (varieties) have been grown as cuttings to give genetically identical clones. The use of cuttings for propagation allows the generation of crops with very narrow ratios of cannabinoid content. GW's first product SativexTM, an oromucosal spray composed primarily of THC and CBD, has been approved by Health Canada (GW Pharmaceuticals Plc, 2007).

When considering bioactive molecules occupying novel chemical space the anti-malarial compound artemisinin stands out. Artemisinin (also known as Qinghaosu) is an extract of *Artemisia annua*, and is a complex 1,2,4-trioxane tetracyclic sesquiterpene (Fig. 2).

Shown to be effective for treatment of malaria by Chinese scientists in the 1970s, artemisinin, as part of an artemisinin based combination therapy (ACT), is now considered to be the leading treatment for malaria in chloroquine resistant areas (WHO, 2006). Large quantities of *Artemisia* are required to meet clinical need. The number of companies extracting artemisinin in China rose from 10 to 80 between 2003 and 2005 and from 3 to 20 in Vietnam. Commercial cultivation also began in East Africa and Madagascar (Kindermans et al., 2007). However, the commercial market for artemisinin is extremely volatile with large fluctuations in price and recently prices have dropped to $200/kg (down from a high of over $1,000/kg in 2004); such low prices caused some growers to switch to more profitable crops (CNAP, 2007; Kindermans et al., 2007). The Centre for Novel Agricultural Products (CNAP) at the University of York (UK) is using fast track breeding techniques to increase yields of artemisinin. With funding from the Bill and Melinda Gates Foundation (CNAP, 2007), they have developed new high-throughput screening methods, which can extract and measure the artemisinin content of plants in minutes. The team eventually aims to screen 25,000 plants generating a collection of individuals with valuable traits.

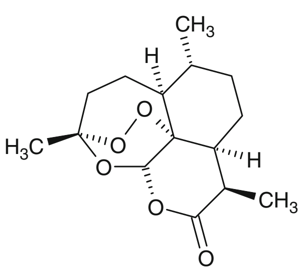

Fig. 2 Artemisinin extracted from *Artemisia annua*

Artemisia annua grows wild in northern Europe. Commercial scale cultivation is being studied by European companies looking at germplasm, agronomy, and requirements for harvesting, processing, and delivery (Botanical Developments, 2006).

Recombinant Proteins and Molecular Farming

Over the last decade, the possibility of using plants as vectors for the large scale production of recombinant proteins and vaccines has moved from development to commercial activity. So called ‘molecular farming’ is seen as an opportunity to overcome the problems of scale-up associated with fermentation or transgenic animal systems. However, over 80% of the production cost of these proteins is associated with downstream isolation and purification of the protein and these downstream costs vary little with production method. Therefore, to compete with simpler rival production methods, the increased cost of plant production must be offset by higher yields of expressed protein (Fowler and Law, 2006; Fisher et al., 2004; Twyman et al., 2003).

Due to its ease of manipulation and significant potential to produce biomass, the tobacco plant (*Nicotiana tabacum* L.) has received a great deal of attention as a candidate for production of recombinant proteins (Epobio, 2007a; Twyman et al., 2003). The European biotechnology company Meristem has developed systems for recombinant protein expression in whole leaf biomass. Proteins under development include gastric lipase and lactoferrin. The Large Scale Biology Corporation also chose tobacco plants for production of a range of therapeutic vaccines and proteins. They have adopted a new approach using viral vectors with the capacity to express genes of interest in non-transgenic plants. These tobacco mosaic virus and related vectors move rapidly throughout the entire plant, causing protein synthesis and accumulation in most tissues. Over the last 50 years, safflower (*Carthamus tinctorius*) has been cultivated mainly for its vegetable oil. Recently, in addition to the production of nutritional oils, SemBioSys Genetics has developed systems for production of insulin and proteins in safflower for use in cardiovascular therapy. These products are currently undergoing clinical trials. The potential for in-plant production of recombinant proteins is clear; however, it remains to be seen whether this production system can compete with microbial fermentation and whether the required GM technology will be accepted by society.

Herbal Medicines

Although single active ingredient pharmaceuticals dominate western medicine, in many parts of the world herbal or traditional medicine forms the mainstay of healthcare. The use of herbal medicine is also growing in both Europe and the US. The global herbal medicine market was worth over €45 billion per year in 2003 and is growing steadily (WHO, 2003). Although often not supported by extensive clinical data, herbal medicines are commonly used for treatment of a wide range of complaints from depression to hypertension. Some preparations have been well studied and have proven clinical effects; these include treatment of moderate depression with St John's Wort extract, garlic for decreasing high blood pressure, the use of *Ginkgo biloba* extract for the treatment of dementia (Bardia et al., 2007; Mar and Bent, 1999). The herbal medicines market is largely served through the wild harvesting of medicinal plants (Williamson and MacTavish, 2007).

There are, however, concerns over the quality and authenticity of some herbal medicines. These concerns have resulted in the European Traditional Herbal Medicinal Products Directive (2004/24/EC) (THMPD) (European Union, 2004). Coming into force in 2011, the Directive will bring consistency and regulation to the herbal medicines market across Europe. In additional to concerns over safety, the increased amount of wild crafting is raising sustainability questions. Of the 40,000–50,000 plant species used in herbal medicines, 70% are wild crafted and 4,000 of those face extinction. The opportunity for commercial cultivation of medicinal herbs has been reviewed (Williamson and MacTavish, 2007). The study identified up to 36 species of plants suitable for cultivation in Northern European agroclimatic conditions or under controlled conditions. The authors reviewed potential volumes and prices and the species with greatest potential for economic development are shown in Table 3.

Whether the commercial cultivation of medicinal plants increases will be largely dependent on how the industry and consumers respond to new regulations such as the THMPD. The costs associated with the Directive may appear to be off-putting to producers, but on the other hand the reassurance provided to consumers and medical practitioners may further stimulate the sector. In addition, the need to grow crops under GAP may help prevent the exploitation of endangered wild species.

Nutrition and Personal Care

In addition to the long standing uses of natural products in pharmaceuticals and herbal medicines, new developments in nutrition and cosmetics continue to provide new opportunities for cultivation of non-food crops. Providing the momentum for developments such as sweet gale is a strong customer drive for products derived from natural sources. This can be seen in the personal care sector in products from shampoo to skin care. The natural cosmetic market is believed to be near the €1billion mark in Europe (Organic Monitor, 2006). Another

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Table 3 Medicinal plant species offering opportunities for commercial cultivation in Northern Europe

Species	Common name	Note	Type of bioactive
Arctostaphylos uva-ursi	Bearberry	Endangered and in demand	Hydroquinones, arbutin, tannis, phenolic glycosides and flavonoids
Atropa belladonna	Deadly Nightshade, Belladonna	Controlled cultivation necessary	Tropane alkaloids
Baptista tinctorum	Wild Indigo	Immune system herb increasingly in demand	Arabinogalactan proteins
Cetraria islandica	Iceland Moss	Endangered species, sustainable cultivation required	Lichen acids (usnic acid) and polysaccharides
Crataegus oxyacantha	Hawthorn	Long term crop with increasing demand	Bioflavonoids, triterpenes, proanthocyanins, polyphenols, coumarins
Gentiana lutea	Yellow Gentian	Endangered, requires cultivation research	Bitter principles (gentiopicriside, amarogentin), gentainose, inulin, phenolic acids
Hydrastis canadensis	Goldenseal	Endangered with increasing demand	Isoquinoline alkaloids.
Orchis mascula and *Orchis morio*	Purple and Green Winged Orchid	Endangered. Sustainable supplies required	
Primula veris	Cowslip, Oxlip	Endangered	Triterpene saponins, flavonoids, phenols
Ruscus aculeatus	Butchers Broom	Endangered	Saponin glycosides
Saponaria officinalis	White Soapwort	Endangered with increasing demand	Saponins
Scutellaria baicalensis	Baical Skullcap	Potential wider applications	Baicalin, baicalein, tenaxin, skullcap flavones
Viola odorata	Sweet Violet	Many application with history of UK cultivation	Phenolic glycosides, saponins, flavonoids, alkaloids, mucilage

new and growing market is functional foods; in 2006, the US functional food market was estimated to value $36 billion (Sloane, 2006). Evidence from epidemiological studies increasingly demonstrates the benefits of plant-rich diets. Identifying the bioactive compounds responsible for these benefits is an active area of research. Compound groups under examination include polyphenols, flavonoids, lignans, stilbenes, salicylates, and sterols (Hooper and Cassidy, 2006).

Many of these compounds are being analysed for antioxidant activity. Antioxidants are an important and growing area in functional foods and the potential for novel antioxidants from plant sources has not gone unnoticed. Tocopherol and ascorbic acid, either synthetic or natural are the most widely used biological antioxidants; most natural tocopherols are isolated from soybean oil whereas ascorbic acid is prepared through a double fermentation process. The antioxidant activity of rosmarinic acid is well known and understood (Chang et al., 1977). Rosemary (*Rosmarinus officinalis* L.) is a member of the Labiateae or mint family (Petersen and Simmonds, 2003). It is a slow growing, cold sensitive, woody perennial cultivated for its aromatic foliage. The crop is widely grown on a commercial scale in Spain, France, Italy, Croatia, Tunisia, and Morocco for its high-value essential oils. The antioxidant potential of rosemary has been recognised since the 1950s. A range of phenols with antioxidant activity has been isolated from rosemary leaves including rosmarinic acid and carnosic acid (Fig. 3). Carnosic acid is known to undergo degradation and rearrangement to a number of derivatives (carnosol, rosmanol, rosmariquinone and methyl carnosate) all with antioxidant activity.

Polyunsaturated fatty acids (PUFAs) such as α-linolenic (ALA) and γ-linolenic (GLA) (Fig. 4) are in high demand by both the nutraceutical and cosmeceutical markets.

Although not produced by the human body, these Essential Fatty Acids (EFAs) are required for normal brain function, growth, development, bone health, stimulation of skin and hair growth, regulation of metabolism, and maintenance of reproductive processes (University of Maryland Medical Centre, 2008). The health benefit provided by PUFAs is dependent on the precise PUFA being taken. The health benefits of the fish derived PUFAs eicosapentanoic acid and docosahexanoic acid are well described (Sanderson et al., 2002). There is interest in whether plant produced PUFAs such as ALA and GLA offer the same benefits. The metabolic profile of GLA and its efficacy in the treatment of several diseases has been reviewed (Fan and Chapkin, 1998). The efficacy of GLA has been noted for the treatment of pain, stiffness, and tender joints in rheumatoid arthritis sufferers (Soeken et al., 2003). A number of non-food crops are cultivated to meet the demand for both healthcare and personal care applications. Oil from hemp (*Cannabis sativa)* seed contains approximately 56% linoleic acid, 22% ALA and 4% GLA (Callaway, 2004). Only cultivars with less than 0.2% of the psychotropic agent THC may be grown for fibre and seed oil production in the EU. Camelina or Gold of Pleasure (*Camelina sativa*) produces an oil high in polyunsaturates (>50%). In addition to high levels of ALA (~40%) and GLA (~15%), the oil also contains antioxidants such as tocopherols. Adaptable to both climate and soil, Camelina has been grown in several European countries and is attracting interest from US growers (IENICA, 2002). When in flower, borage (*Borago officinalis*) is a distinctive blue crop. It is grown for its high concentrations of GLA, which accounts for 20–23% of its oil content. The oil, branded as Starflower Oil can be found in health foods, skin care creams, and cosmetics. The global requirement for borage oil has been estimated at around 1,500 t.

Croda Chemicals Europe Ltd. has developed Echium oil from *Echium plantagineum* for use as

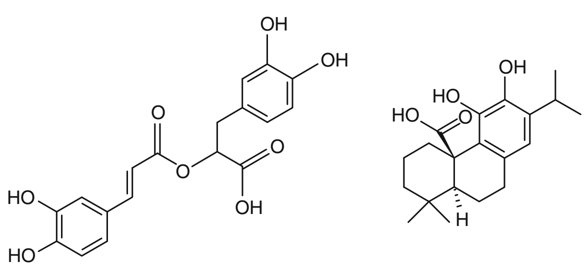

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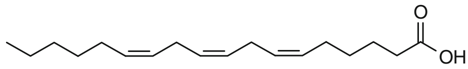
Fig. 3 Antioxidants, rosmarinic acid (1) and carnosic acid (2)



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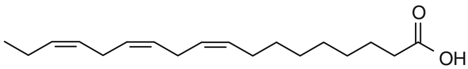

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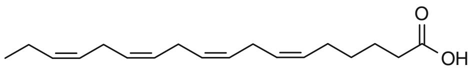

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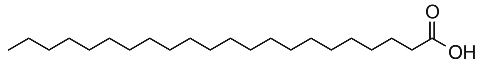
Fig. 4 Polyunsaturated fatty acids, γ-linolenic acid (1), α-linolenic acid (2) and stearidonic acid

a functional food. Echium contains high levels of several EFAs including GLA (9–12% of oil content). Despite the interest in GLA, it is the high levels of stearidonic acid (Fig. 4), with demonstrated anti-inflammatory properties, which make the extract of particular interest. The use of stearidonic acid in anti-wrinkle creams and sun aftercare make the oil attractive to the personal care market. Studies on stearidonic acid as treatment for eczema, acne and other skin disorders may lead to its medicinal use.

Many of the ingredients used in cosmetics and household cleaning products are products of the oleochemical industry. Of particular importance for the cosmetic sector is coconut and palm kernel oil because of their high percentage of fatty acids with short to medium chain length (mainly lauric acid C12 and myristic acid C14). These fatty acids are particularly suitable for conversion to surfactants for cosmetic and washing agents.

Also used in surfactant production, betaine is isolated from sugar beet as a value added co-product from sugar refining. Betaine is used in skincare formulations as a moisturiser and stabiliser for its water binding and cell membrane protecting properties.

Behenic acid (Fig. 5) is a major component of Ben oil (or behen oil), from the seeds of the Ben oil tree (*Moringa oleifera*). The Ben oil tree is widely cultivated in tropical Africa and America, Sri Lanka, India, Mexico, Malabar, Malaysia and the Philippine Islands as a food crop. Although behenic acid is also present in other oil-bearing plants, including OSR and peanut, it is produced commercially using erucic acid (Fig. 5) from high erucic acid varieties of OSR. Behenic acid is converted to a salt and used as a conditioner in hair products.



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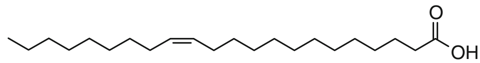

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Fig. 5 Fatty acids, behenic acid (1) and erucic acid (2)

The use of natural oils as cosmetic ingredients is increasing globally. Apricot oil, yuzu (a Japanese citrus fruit) and raspberry extracts form part of a lipstick formulation developed by Kanebo which is claimed to stimulate microcirculation giving a deeper, redder colour. Extracts from orange, almond, carrot and many other plants are finding their way into a range of personal care products. Cognis Care Chemicals have launched a new hair product based on vegetable derived proteins. The complex includes wheat protein Gluadin W 40, Gluadin Soy and wheat micro protein Gluadin® WLM, which due to its low molecular weight (below 1 kDa) is claimed to penetrate, strengthen, and protect hair.

Plant Protection Products

Many secondary metabolites are produced in response to insect challenge. Identification and extraction of these natural products, many of which act by altering insect feeding patterns, presents opportunities for the development of crop protection products. Extracts of the neem tree (*Azadirachta indica*) containing azadirachtin have been studied and used extensively for crop protection. A wide range of plant extracts with insect anti-feedant activity are known including thyme (*Thymus vulgaris*), ashwagandha (*Withania somnifera*) and checkerberry (*Gaultheria procumbens*) (Isman, 2002). Rotenone is a natural insecticide obtained from the roots of several tropical and subtropical plant species belonging to the genera *Lonchocarpus* or *Derris*. A regulated plant protection product, rotenone can be used in organic farming practice. Carvone, a volatile terpenoid component of caraway oil (*Carum carvi*), has been shown to suppress sprouting of potatoes during storage, being marketed in the Netherlands for this purpose as the product 'Talent'. Large scale development beyond niche markets for plant-derived plant protection products is hindered by development costs and regulatory requirements.

Oil Crops for Industrial Applications

Oil crops are not restricted to nutritional or personal care applications. Driven by environmental regulations plant-based oils have found applications in areas such as cutting fluids, chainsaw lubricants, metal working fluids, hydraulic oils and 2-stroke engine oils. Around 90% of industrial and commercial lubricant applications can be satisfied by the newer generations of biolubricants derived from crops like OSR and sunflowers (Schneider, 2006). To overcome technical issues with OSR biolubricants, new cultivars with specific fatty acid profiles have been developed. High oleic acid rape varieties containing low linolenic acid levels have been developed, known as HO, LL varieties. This oil has improved oxidative stability allowing its use as a lubricant in higher temperature applications.

OSR varieties (HEAR) containing high levels of erucic acid have also been developed. Erucic acid is used in numerous applications (Gunstone and Hamilton, 2001) but its primary use is through conversion to erucamide for use as a plastic slip agent. HEAR varieties contain 40–50% erucic acid as a percentage of the oil. Crambe (*Crambe abyssinica*) also known as Abyssinian mustard, is a new introduction to UK agriculture (Epobio, 2007b). Prevalent across Asia and Western Europe, it requires moderate rainfall and warm temperate conditions. Crambe is grown for its high content of erucic acid (~56% of oil content) and provides advantages over HEAR for production of erucamide.

Concluding Remarks

From fatty acids to steroids and proteins, crops can provide us with a wide range of ingredients for healthcare, personal care and industrial materials. Increasing consumer demands for natural ingredients, concerns over environmental issues and the increasing price of crude oil is creating a commercial climate ripe for the development of renewable and sustainable non-food crops. Hurdles do need to be overcome in order to develop stable markets and secure supply chains. Ranging from improved understanding of non-food crop agronomy through to regulatory requirements for production and use, the sector requires coordinated development. Food crop yield and quality has increased dramatically throughout the second half of the twentieth century, whether this trend will be sustained and whether this success can be transferred to non-food crops remains to be seen. Other issues relevant for the sector will be developments on yield and natural product output plus the routes to development of optimised crop varieties. Sustainable non-food crops can be used to deliver industrial sustainability, cut our greenhouse gas emissions, improve rural economies, and increase crop biodiversity. If current consumer demand, high oil prices, and political support are maintained we can expect to see a further and significant increase in the cultivation and use of materials from non-food crops in everyday life.

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