EIP-AGRI Focus Group

Plant-based medicinal and cosmetic products

MINI PAPER 6. Knowledge and technical needs in production of the raw material

Guillaume Frémondière, Silvana Nicola; Willemijn de Jongh, Katerina Grigoriadou, Andrea Primavera, Dimitrios Argyropoulos

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1. Introduction

Many of the Medicinal and Aromatic Plants (MAP) species are cultivated in very small areas.. The whole production of more than 150 different species in the European Union–is less than 0.1% of the whole agricultural area.. For that reason, MAP growers are faced with important technical challenges to produce plants and active compounds as efficiently as possible in the respect of the consumers' needs.. Because MAP growers are cultivating orphan species, few or even no technical support is available for them.

2. State of the art

The production scheme of MAP species is more or less very similar to other plant species and is divided in 4 main steps: (i) the genetic material, (ii) the propagation of this material, (iii) the cultivation of this material and (iiii) the collection of this material. At each step, the grower has to take many parameters into account in order to produce raw material according to the industrial needs for a quality, quantity and economic point of view.

The genetic material

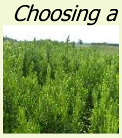
The species

. A species is chosen by the grower based on its' suitability for productionSame active compounds can be produced by many species like rosmarinic acid in rosemary or in lemon balm. In this case, the name of the active compound is confusing because lemon balm will give you better results. French tarragon is much more aromatic than Russian tarragon selection of the right variety has consequences for the end product.

The variety

A species can be composed of different varieties with totally different traits. It is important to choose the variety adapted to your market, your pedoclimatic conditions, your material, ….

Choosing a variety may have technical impact directly for the growers. For example :



Considering different variety of rosemary, the variety Golden rain will be perfect to get a very nice colorful spreading plant for ornemental purposes while Sudbury blue will be very suitable with production of carnosic acid and Upright will be perfect to produce dry aromatic herbs for cooking

Some thyme varieties can be directly sown in the fields and cropped as an annual crop (Deutscher Winterthymian), some others have to be sown in nursery before plantation (Carvalia, Varico 3, …) and some others are only vegetatively propagated (T36, L2, …).

Considering the legal aspects, A fennel (Foeniculum vulgare) variety with low estragol content such as Fenulia is preferable compare to another one with high estragol content , the same t applies to THC content for Cannabis sativa.

In order to enhance the productivity, a first selection has been made among the genetic resources available in botanical gardens and genebanks. Improvement of this wild selected material has been performed thanks to variety breeding. As the breeding method can be used to create new variety and those varieties are proposed to growers via specific companies such as Mediseeds in Switzerland, Pharmasaat in Germany or Iteipmai in France. Variety breeding permits enhanced yield in biomass, the standardization of secondary metabolites, the tolerancy to biotic and abiotic stress, etc.

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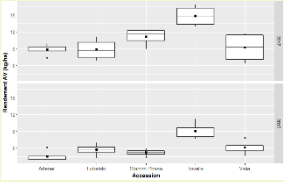
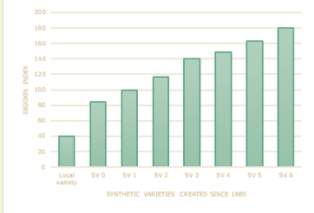
Breeding adapted varieties has permitted to upgrade different species such as :

Valeriana officinalis with an increase of 30% of the roots biomass	*Salvia sclarea with an increase of 30% of the level content of sclareol*	*Digitalis lanata with 4,5 times more digoxin compared to local variety*	*Ocimum basilicum Genovese style with a higher tolerance to downy mildew and many others species*






The breeding adapted varieties has permitted to upgrade different species such as, (Fig 1), Nevertheless, according to the size of the market, few companies are directly involved in the MAP variety breeding and most of the breeding program are supported by a part of public funding.

Propagation

Seeds multiplication

Like many other species, seeds are used by both growers and nurserymen to multiply plant material. Different strategies can be used to propagate those seeds: seeds to seeds propagation, parental lines, polycross of parental clones, seeds production on male sterile clones, etc. Every type of seed propagation scheme has to be followed very carefully in order to avoid genetic deviation from the original variety. Morphological controls, genetic control and phytochemical controls can be performed at every stage to warrant the authenticity of the variety. Germination level is also a key point, indeed, the propagation of the variety and the way to manage the production is directly correlated to the number of plants and, therefore, the germination level. It has to be tested before sales during all the life of the seeds that can differ from one species to another e.g. loss of 50% of the level of germination on many *apiaceae* in 2 years.

Vegetative propagation

This type of propagation is very common in the MAP productions. It permits to replicate one mother plant in several daughter plants strictly identical to the original plant. It cans be done a traditional way or with tissue culture techniques (fig 1). Thanks to this clonal multiplication, the specificity and advantages of the mother plant are kept a uniform way and the quality you are supposed to get at the harvest time is very stable. E.g. *Lavandula intermedia*, *Rosemarinus officinalis*, *Pelargonium roseum*, *Mentha piperita*, are propagated this way. While using this type of technique to multiply vegetal material; sanitarian problems may occur. Indeed, a large range of pathogens and especially viruses and phytoplasms can also be propagated this way. To reduce the risk, a strong traceability is needed. Official propagation schemes are undeveloped in the MAP sector. Only the French lavender and lavandin technical certification does exist. This regulation is not compulsory but permits to control the production of plantlets and seedlings of lavender and lavandin on every stages of the production from the sanitarian and the genetic point of view. This type of control permits to enhance the production and reduce the disease pressure. Promotion of these Good Practices of Propagation on other species, would give important benefits and advantages to growers.

Figure 1 : Clary sage vitroplants

Fig 2 : Certification label for Lavandula sp.

Cultivation practices and techniques:

Implantation of the crop

Depending on the material of propagation and depending on the constraints of the species, different strategies can be used: mono row plantation (*Rosemarinus officinalis, Valeriana officinalis*, …), multiple rows plantation (*Thymus vulgaris, Chamaemelum nobile*, …), mono row sowing (*Lavandula angustifolia*), full sowing (*Ocimum basilicum, Papaver somniferum, Angelica archangelica*, …). For species the can be implanted different ways, the use of plantlets produced by nurserymen is often the choice of the growers. Indeed, row plantation is much easier to control weeds with mechanical tools.

The density is also very important to optimize the production.

Nutrient needs

The nutrient importation and exportation of the MAP species are not very well known. Nowadays, most of the fertilization on MAP species is done according to oral transmission and growers experiences. Except for few examples like nitrogen on opium poppy (*Papaver somniferum*) or sulphur needs on *liliaceae*, the level of knowledge on nutrient needs for MAP species is very low. As secondary metabolites are very important for MAP production, enhancing biomass production is not a key answer if the level content in secondary metabolites is reducing at the same time. Fertilization programs have to be built considering those two aspects.

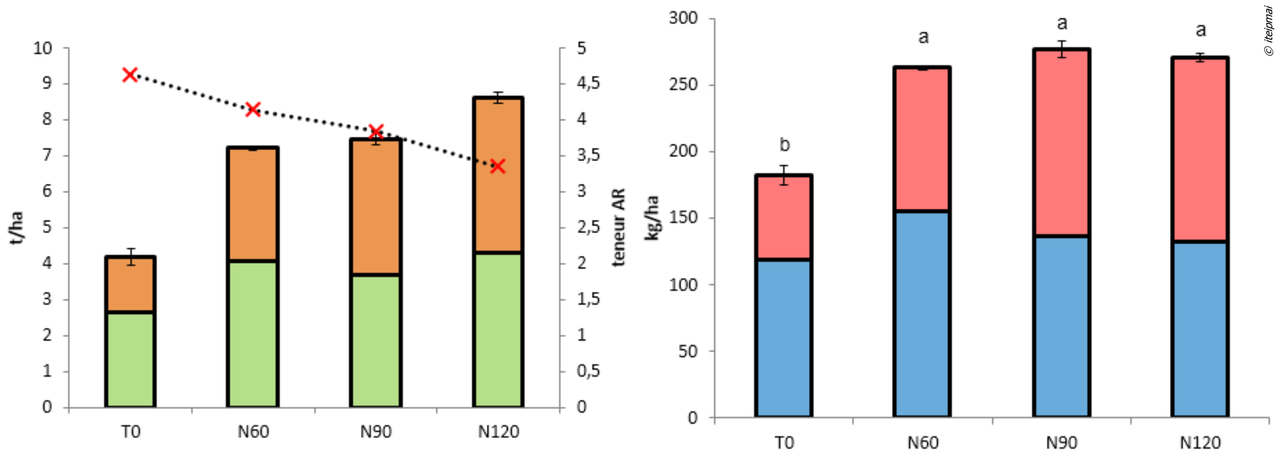


Figure 3 : Evolution of the level content of essential oil and yield in essential oil depending under different nitrogen fertilization inputs in Melissa officinalis

Pest control

The width of MAP species range is very important and each species has its own pest or disease problem but a transversal need for MAP growers is sustainable weed management. On conventional culture, up to 150 hours per hectare are needed to keep the level of weeds, which impact yield/quality, low on medicinal plants. For perfume plants, the cost of the hoeing represents 10% of the turnover. On organic production, those figures are easily doubled (or more). Weeds have a direct impact on the yield but also on the quality (more sorting, dilution, contamination with foreign secondary metabolites, …) and on the Human health. Indeed, weeds like *Senecio* spp or some *Boraginaceae* produce toxic alkaloids (pyrrolizidinic alkaloids: PA) and EFSA (European Food Safety Agency) recommends to intake maximum 1 µg PAs per day for a 50 kg person. Those plants are very common in production plots and only five plants per hectare will give a positive result thanks to modern detection techniques. Moreover, because of the translocation of those PA, the weeds have to be removed from production plots, which is very expensive.

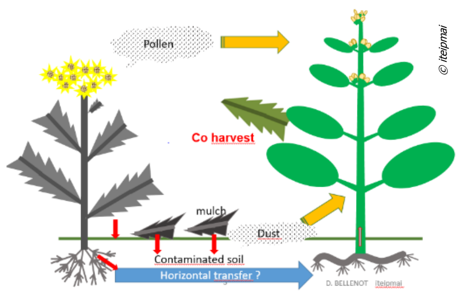


Figure 4 : Transportation of PA from weeds to plants of interest

According to the lack of phytosanitarian solutions (conventional, biocontrol, alternatives, …), growers needs to adapt their crop management to reduce the sanitarian pressure or use tolerant varieties. For some specific species, some disease can destroy the crop like downy mildew on basil (*Peronospora belbarhii* on *Ocimum basilicum*) or dramatically reduce the potential like Stolbur on *Lavandula angustifolia*. To control those pests, genetic solutions with tolerant variety is part of the key to reduce the occurrence of the disease. Nine new Genovese style basil varieties has been released in 2018 and seems to be cropable with low/no phytosanitarian inputs; 80% of the seeds propagated *Lavandula angustifolia* in France is represented by selected varieties. Moreover, vigorous varieties might grow faster than weeds and thus reduces the cost of hoeing, for example a new candidate variety of *Valeriana officinalis* that has a quick development, reduces the time of manual hoeing by 30% compared to standard varieties in organic production.

Furthermore, decision supporting system that can predict the apparition of diseases are very relevant to manage crops. It permits to anticipate a risk and manage it by spraying, harvesting, covering … the crop of interest.

Fig. 5 : Archangelica archangelica under clover

Cropping systems

The way MAP are cropped is also very important to be sure to get the best output for your market according to your machines and facilities. Alternatives techniques like cover crop are very new on MAPs but can have strong impact. For example, on *Lavandula* spp, every type of cover crop reduce by 50% the trapping of *Hyalesthes obsoletus* (vector of Stolbur) ; implantation of *Angelica archangelica* in a living clover field ensure equivalent yield as a standard management but with a hoeing time divided by 3.

Harvesting practices

Harvest management

Determineing the right moment and the right part of the plants to harvest is really important to get the optimal yield. Indeed, in MAP production, secondary metabolites are often the most important. The content of those metabolites is very heterogeneous during the year and they are not synthetized in the whole plants but only in some specific organs : flowers (calix) for *Lavandula angustifolia*, roots for *Valeriana officinalis*, whole plants with roots for *Arnica montana*, …

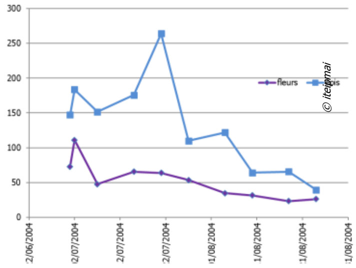


Fig. 6 : Evolution of the level content of essential oil in Lavandula angustifolia depending on the harvest organs and the maturity stage

Machinery

As for the other type of machine, MAP are suffering of the size their market represents for harvester makers.

Figure 7 : Espieur, harvesting machine permitting to separate flowers from stems

Most of the time, growers are adapting machine that are not build for MAP purpose: small potato harvester for many root MAP ; young plants harvester for herbs, … Even if for big areas, some specific harvester can be found in commerce, small grower has often no alternatives than self-construction. As the collection of the proper organ is very important to get the best yield, the harvester has to be adapted to reduce the non-interesting parts of the plants like stems from the flower stalks of *Lavandula* spp. By adapting the harvester with this type of consideration, agricultural costs will be reduced but also transport costs and post-harvest process costs.

Cultivation under cover

Greenhouses and glasses houses

Growing MAPs under cover facilitates the environmental conditions, allowing earliness and enhanced yield. However, the covering material must be checked for quality of light transmittance to avoid missing important wavelengths for metabolite synthesis. Under protection such as greenhouses and tunnels, plants are cleaner and with less microbial spoilage. Attention must be paid to include bumble bees if the crop requires pollination.

Soilless Culture, Vertical farming (aeroponic, hydroponic)

MAPs grown in soilless culture systems is increasing. Traditional soilless culture system is used for herbs, generally grown in pots. From nursery production to commercial pot production, substrate-based soilless growing systems are common in many Mediterranean countries and also in Northern European countries. More modern, advanced and sustainable systems are in hydroponics (such as Nutrient Film Technique, Floating systems, aeroponics) for high yield, recirculating systems and saving inputs. Example of aeroponic systems used for MAPs is for producing saffron. The ultimate system is the indoor farming, including vertical farming system: they are spreading in a number of cities, for fresh delivery of herbs.

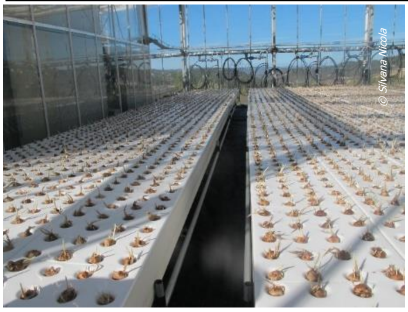


Figure 8 : Different types of soilless productions
A - Herbs grown in pots
B - Basil production in floating growing systems
C - Mint production in a NGS system
D - Saffron production in aeroponic systems
E - Basil production in vertical farming

Advanced techniques

Bioreactors

Plant cell and tissue culture technology has been considered a powerful tool for the biomass and bioactive compound production from medicinal plants. Cell cultures can offer several potential advantages over the extraction of compounds from field grown plant material

- Continuous production systems independent of geo-graphical or environmental variations and constraints. Products of uniform quality produced from defined
- Good Manufacturing Practice (GMP) systems that can be guaranteed free of agrochemicals
- The possibility for high concentrations of target compounds and rapid production of biomass. In nature the target compounds may be only found at low concentrations or in specific plant tissues
- Easier extraction protocols, reducing the need for use of aggressive solvents.

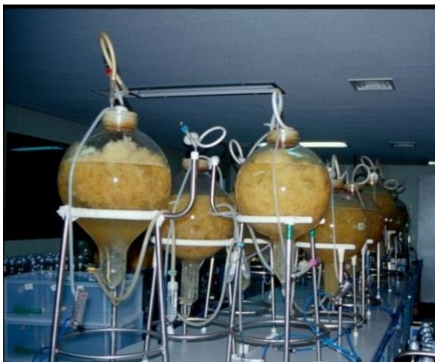


Figure 9: Ginseng root production in bioreactors in Korea

The use of the plant tissue culture process has been proved a potential alternative for more efficient production of some compounds and active ingredients (eg ginseng saponins - fig 9). Cell culture may also offer better selectivity and yield for the desired bioactive products, since the cell strains may be selected from tissue or organs can be more productive than other parts of the plant.

Hairy-roots cultures

Hairy-root cultures (HRs) are a very promising alternative to the biotechnological exploitation of plant cell cultures. The principle is to grow plants in a specific indoor system. The plants follow different non-destructive steps. They are planted and stimulated (nutrients, chemicals, light, etc) to produce secondary metabolites. Their roots are bathed in an adapted solvent to extract those secondary metabolites. Then plants get back to "stimulation stage" while metabolites are purified. Different technologies are already in motion such as PAT® (**www.plantadvanced.com**). This technologyis fifty times more productive than open fields production. Indeed, one green house produces as much metabolites as 1000hectares of fields.

3. Research needs from practice and innovative ideas

Theme	Task	Description and ideas
Tools to enhance the genetic diversity	Characterization of the actual gene banks	Phenotyping, genotyping and characterization of genebanks Creating core collections (maximum of genetic variation in the minimum of accessions).
	Improvement of the genetic material	Promoting variety creation thanks to updated breeding technologies Developing adapted genetic tools to MAP species Supporting variety breeding programs that includes multifactorial aspects For example Epigenetics.
Promotion of the knowledge on the plant needs to grow and/or to produce secondary metabolites	Pedoclimatic conditions	Developing new innovative crop management under climate changes especially for species cultivated under extreme type of conditions (Mediterranean, Alpin, …) Understanding of the physiology of the plants to stimulate the biosynthesis of secondary metabolite
	Nutrient inputs	Determining the nutrient requirements for MAP species to optimize the production of secondary metabolites. Developing ready-to-use tools to control the quality of the crops (sanitarian diagnosis, optimal stages for harvest, …) Creating a pictures database of weeds of MAP species to be used by Artificial Intelligence Developing biocontrol solutions for MAP species and use of MAP species as biocontrol solutions
	Bioreactors and Hairy-Roots	Understanding the underpinning biological mechanisms that control the target metabolite biosynthetic pathways
Mechanization and automation	Plantation	Developing specific machines for the plantation of cuttings and the harvest of the rooted plants
	Crop management	Developing machines (robots, AI, precision farming,…)to discard all the weeds Testing cover crop species to avoid implantation of the weeds. Stimulating and eliciting MAPs thanks to light (wave length, infra red, UV, …) especially for under cover productions.
	Harvesting	Developing harvest machines that pick up only the interesting organs
Decision supporting systems		Developing tools to determine the optimal stages of harvest r the phytosanitarian status of a plant. Developing mathematic models to predict apparition of a disease or the emergence of an insect

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4. Ideas for new Operational Groups

Theme	Description
Variety breeding tools	MAP core collections, transfer of molecular tools in MAP, transfer of new breeding technologies in MAP. Enhancing traditional systems.
Good practices for seeds and plant production	Gene bank management (nomenclature, traceability, quality control, …), standard genealogical selection scheme for different MAP species models, databases, seeds production optimization, transfer to nurserymen
Machinery and advanced technologies	Address book of machine builder (hoeing, harvesting, …), sensor – captors for the recognition of (i) weeds in MAP crops (ii) organs of interest of the MAP crops
Weeds management via alternative techniques	Cover crop management, which cover crop for which MAP
Contaminant weeds	Weeds life cycle, management strategy, weeds description and classification, recognition index
Quick diagnostic on MAPs	Tools to control plants quality in fields, decision supporting systems, …
Drought and hydric stress management	Evolution of climate, adapted species and varieties, understanding on physiological behavior of MAPs, crop management adapted to reduce stresses
Biocontrol with MAPs and other uses of MAPs	Knowledge on chemotypes, adaptation of the chemotypes according to the target (on plant production, on animal production, on agro food industries, …), uses of MAPs as companions plants, …
Enhancing secondary metabolites production	Knowledge on physiology and ways optimize crop management

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AGRICULTURE & INNOVATION

The European Innovation Partnership 'Agricultural Productivity and Sustainability' (EIP-AGRI) is one of five EIPs launched by the European Commission in a bid to promote rapid modernisation by stepping up innovation efforts.

The **EIP-AGRI** aims to catalyse the innovation process in the **agricultural and forestry sectors** by bringing **research and practice closer together** – in research and innovation projects as well as *through* the EIP-AGRI network.

EIPs aim to streamline, simplify and better coordinate existing instruments and initiatives and complement them with actions where necessary. Two specific funding sources are particularly important for the EIP-AGRI:

- ✓ the EU Research and Innovation framework, Horizon 2020,
- ✓ the EU Rural Development Policy.

An EIP AGRI Focus Group* is one of several different building blocks of the EIP-AGRI network, which is funded under the EU Rural Development policy. Working on a narrowly defined issue, Focus Groups temporarily bring together around 20 experts (such as farmers, advisers, researchers, up- and downstream businesses and NGOs) to map and develop solutions within their field.

The concrete objectives of a Focus Group are:

- ✓ to take stock of the state of art of practice and research in its field, listing problems and opportunities;
- ✓ to identify needs from practice and propose directions for further research;
- ✓ to propose priorities for innovative actions by suggesting potential projects for Operational Groups working under Rural Development or other project formats to test solutions and opportunities, including ways to disseminate the practical knowledge gathered.

Results are normally published in a report within 12-18 months of the launch of a given Focus Group.

Experts are selected based on an open call for interest. Each

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