

Unit 5: Fermentation Technology

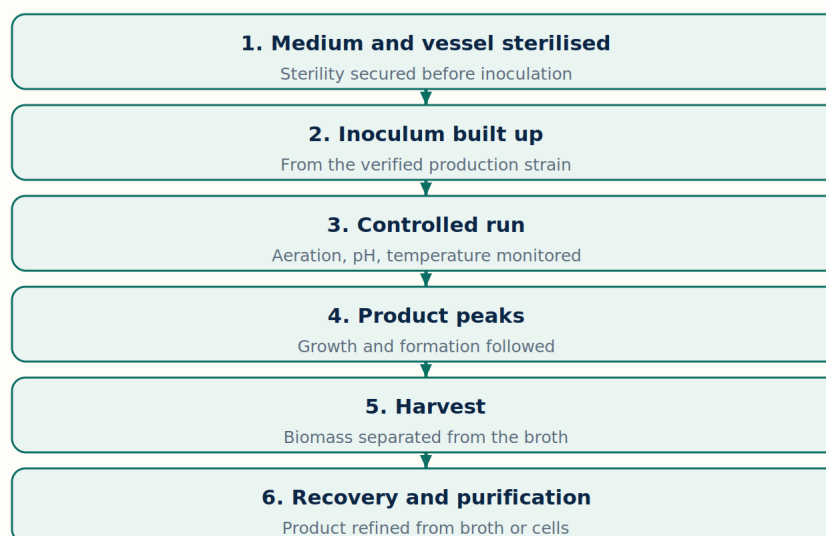
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5.1 Application of fermentation technology

Fermentation technology, in the broad pharmaceutical sense used by this unit, is the controlled large scale culture of organisms, classically microorganisms, and their use as producers of useful compounds: the organism is grown in a fermenter on a chosen medium under monitored conditions, and the product is recovered from the broth or the biomass. Its applications across pharmacy are the frame for the three named products that follow: antibiotics and other microbial medicines historically defined the industry; organic acids, solvents and amino acids serve as industrial and pharmaceutical intermediates; vitamins and steroids transformations serve drug manufacture; and the products this unit names, ergot alkaloids, single cell proteins and enzymes, represent its medicinal, nutritional and catalytic faces. Plant biotechnology meets fermentation at two points already taught: the plant cell bioreactor of Unit 4 is fermentation hardware and thinking applied to plant cells, and conversely the microbial fermenter is the scale model every culture technology imitates, with its inoculum train, sterilised medium, controlled aeration, pH and temperature, timed harvest and downstream recovery. The general flow below states that shared sequence in its classical microbial form.

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Prepare and sterilise the medium and the fermenter
|
Build the inoculum from the verified production strain
|
Inoculate and run the fermentation under controlled conditions
|
Monitor growth and product formation through the run
|
Harvest at peak product; separate biomass from broth
|
Recover and purify the product from broth or biomass
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The fermentation flow



The controlled run makes the product; recovery decides its quality

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Figure: The fermentation flow. The controlled run in the middle is where the product is made; sterilisation before it and recovery after it decide whether that product reaches the market.

5.2 Production of ergot alkaloids

Ergot is the sclerotium of the fungus *Claviceps purpurea*, which parasitises rye and other grasses, and its alkaloids, built on the lysergic acid nucleus, include compounds of established obstetric and migraine medicine, ergometrine and ergotamine being the classical named examples of the pharmacopoeias. Fermentation production exists because field ergot is the least controllable of drug supplies: yield and alkaloid profile depend on the host crop, the fungal strain and the weather, and the sclerotia carry a variable mixture of wanted and toxic alkaloids. In fermentative production a selected high producing strain of the fungus is grown in submerged culture on a suitable medium under controlled conditions, the alkaloids are formed during the run, and the products are recovered from the culture and purified, with strain improvement, medium design and process control replacing the field variables. The teaching points are the contrast and the caution: the contrast, fermentation converts an erratic parasitic harvest into a contained, improvable process, the same argument Unit 1 made for plant cell culture; the caution, the ergot alkaloids are potent and toxic in overdose, ergotism being the classical poisoning of contaminated grain, so production, handling and assay are matters of strict control. Ergot is also the bridge example of the unit: a drug of a lower plant, a fungus, produced by the fermentation technology this subject shares with pharmaceutical microbiology.

5.3 Single cell proteins

Single cell protein, SCP, is the dried biomass of microorganisms, bacteria, yeasts, fungi or algae, grown at scale and used as a protein source, the name referring to the single celled or filamentous microbial producer rather than to any single protein. Production follows the fermentation flow of Section 5.1 with its own emphases: a fast growing, protein rich, non pathogenic producer is grown on a cheap and abundant substrate, historically including molasses, whey, and hydrocarbon or alcohol feedstocks in the classical processes, the biomass is harvested, washed, treated to reduce its nucleic acid content, and dried. The pharmaceutical and allied interest should be stated accurately: SCP serves mainly as food and feed protein, supplementing conventional agriculture from substrates and land it does not compete for, and within this subject it teaches the scale economics of microbial culture in their purest form, where the product

is the cell itself. Its quality questions are also its examination points: nucleic acid content must be controlled because excess dietary nucleic acid burdens purine metabolism; the producer must be free of toxins and pathogens; and the biomass must be digestible and acceptable. Spirulina type algal biomass, familiar from the nutraceutical study of Semester 1, is the algal face of the same idea. SCP therefore closes the loop of the unit: fermentation can deliver a defined molecule, as with ergot, or the producing cell itself, as here.

5.4 Enzymes of pharmaceutical interest

Enzymes of pharmaceutical interest are produced by fermentation because microbial culture is the practical source of enzyme protein in quantity, purity and reproducibility: a selected producer strain is fermented, and the enzyme is recovered from the broth if it is secreted, or from the harvested cells if it is intracellular, then purified, stabilised and standardised by its activity, the measure in which enzymes are always sold and used. The classes of interest should be grouped by their pharmaceutical role. Digestive and replacement enzymes, such as amylases, proteases and lipases of microbial and other origin, serve in digestive preparations and in processing. Therapeutic enzymes used as drugs in their own right, with the classical teaching examples drawn from microbial and plant sources together, include the thrombolytic and anti inflammatory enzymes of the standard texts. Analytical and diagnostic enzymes serve the laboratory, in the reagent systems that measure glucose and other analytes. Industrial and processing enzymes serve manufacture, in food, textile and pharmaceutical processing, and as the catalysts of the biotransformation steps that industry prefers to harsh chemistry. Two quality ideas govern the whole group and close the subject fittingly: an enzyme product is standardised by activity under stated conditions, not by weight alone, and its production strain, fermentation and recovery must be controlled so that activity, purity and safety arrive together, the same discipline of verified starting material, controlled process and tested product that runs from the medicinal plant field of Semester 1 through every culture and fermenter of this subject.

Frequently Asked Questions

Q: What is MPG201T in M.Pharm Pharmacognosy? MPG201T is Medicinal Plant Biotechnology, the first theory subject of M.Pharm Pharmacognosy Semester 2 under the PCI syllabus. It carries 4 credits and 60 hours, taught at 4 hours per week for 100 marks. Its unit hours are not uniform: Unit 1 carries 12 hours, Units 2 and 3 carry 15 hours each, Unit 4 carries 13 hours and Unit 5 carries 5 hours.

Q: What is totipotency and why does it matter in plant tissue culture? Totipotency is the capacity of a living plant cell to regenerate a whole plant, because it carries the complete genome of the organism. It is the foundation of tissue culture: explants, callus, protoplasts and single cloned cells can all, under the right medium and growth regulator conditions, be grown back into complete plants.

Q: What are the stages of micropropagation? Stage 1 is establishment of a surface sterilised explant from an authenticated mother plant in sterile culture. Stage 2 is multiplication of shoots through repeated subculture. Stage 3 is rooting of the separated shoots. Stage 4 is acclimatisation or hardening, in which the plantlets are weaned to soil and normal humidity. Disease indexing and clonal fidelity checks run across all stages.

Q: How do organogenesis and somatic embryogenesis differ? In organogenesis, shoots or roots form separately, and a shoot must still be rooted before it is a plant. In somatic embryogenesis, somatic cells form embryo like structures with both shoot and root poles in one body, which can germinate directly into a plant. Somatic embryos are also the propagule used inside synthetic seeds.

Q: What are hairy root cultures and what are their advantages? Hairy root cultures are roots induced by transfer of *Agrobacterium rhizogenes* genes into plant tissue, grown in liquid culture without added growth

regulators. They grow fast for plant tissue, are genetically and biochemically stable, remain differentiated so they keep root specific metabolite pathways, and suit production of root derived medicinal constituents.

Q: What is somaclonal variation? Somaclonal variation is the genetic and epigenetic variation arising among cells and regenerated plants during culture, caused by the stress of dedifferentiation, growth regulators and prolonged culture. It is a defect in propagation work, where clonal fidelity is required, and a resource in improvement work, where it generates variants from which high producing lines can be selected.

Q: How do precursors and elicitors increase secondary metabolite production? A precursor is a pathway building block fed to the culture to relieve a supply limit, such as an amino acid fed to an alkaloid pathway. An elicitor is a signal that mimics stress or microbial attack, such as a fungal preparation or a jasmonate, and switches the defence related metabolite pathways on. Precursors supply material; elicitors issue the order to produce.

Q: What is cell immobilization and when is it useful? Immobilization confines living plant cells in or on a support, most often by entrapment in a gel such as calcium alginate, while medium flows around them. It is useful where the product is released into the medium, where long production runs and cell reuse are wanted, and where fragile cells need protection from shear, provided diffusion through the matrix does not limit the cells.

Q: What is the role of PCR in plant genome analysis in this subject? PCR amplifies a chosen DNA segment in vitro using two primers and a heat stable DNA polymerase. In plant genome analysis it verifies transferred genes in regenerated plants, amplifies genes and diagnostic regions for cloning and sequencing, supports identity and fidelity studies of species, varieties and micropropagated lines, and, applied to RNA copies, reports whether a pathway gene is switched on.

Q: Are the MPG201T unit wise PDFs free to download on PharmacoLearn? Yes. PharmacoLearn provides the MPG201T notes as free unit wise PDF downloads, one PDF for each of the five units, with the frequently asked questions appended to the Unit 5 PDF. The same page carries the complete notes for M.Pharm Pharmacognosy Semester 2 students.

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