

TABLE 13.1 Examples of Plant Products of Potential Commercial Interest

Pharmaceuticals:

Ajmalicine, atropine, berberine, camptothecin, codeine, diosgenin, digoxin, L-dopa, hypericin, hyoscyamine, morphine, phototoxin, sangranine, scopolamine, Taxol, ubiquinone-10, vaccines, vincristine, vinblastine

Food Colors or Dyes:

Anthocyanins, betacyanins, saffron, shikonin

Flavors:

Vanilla, strawberry, grape, onion, garlic

Fragrances:

Jasmine, lemon, mint, rose, sandalwood, vetiver

Sweeteners:

Miraculin, monellin, stevioside, thaumatin

Agricultural Chemicals:

Allelopathic chemicals, azadirachtin, nerifolin, pyrethrin, rotenone, salannin, thiophene

understood in comparison to animal or bacterial systems. Because of the difficulty of finding and recovering genes from unrelated pathways, genetic engineering using more easily grown organisms to make these products is not now an attractive alternative to plant cell culture. Plant cell tissue cultures have low volumetric productivities, so higher-value products ($\geq \$500/\text{kg}$) are reasonable targets. Thus, the chemicals of greatest commercial interest must be of intermediate to high value and unique to the plant kingdom.

A good example of bioprocess development using plant cell cultures is for the production of the important anticancer agent, paclitaxel (Taxol). Supply problems greatly impeded the clinical development of this drug. Initially paclitaxel was produced by extraction from the bark of the Pacific yew tree (*Taxus brevifolia*). It required three 100-year-old trees to supply enough paclitaxel to treat one patient. This tree is relatively uncommon, and its harvestation had significant adverse environmental impacts. Harvestation of whole trees has been replaced by a method of semisynthesis. Needles and branches of more common yews can be collected, a precursor compound extracted, and the precursor chemically converted to paclitaxel. The collection of needles and branches can be done in a way to prevent death of the plant. However, there are environmental concerns with both needle collection and disposal of solvents from the chemical processing. Production of paclitaxel in large-scale bioreactors provides a product with fewer contaminants, is highly controllable and reproducible, and is environmentally friendly. Commercial production of paclitaxel using large-scale bioreactors is now a reality. Suspension cultures in stirred tank vessels of about 30000 l are used.

The factory production of chemicals from plant cell tissue culture offers a number of important advantages:

1. Control of supply of product independent of availability of the plant itself.
2. Cultivation under controlled and optimized conditions.
3. Strain improvement with programs analogous to those used for microbial systems.
4. With the feeding of compounds analogous to natural substrates, novel compounds not present in nature can be synthesized.

The production of the dye, shikonin, further illustrates these advantages. Japan could not grow sufficient *Lithospermum* to supply its needs, nor was it assured of a stable supply to