

secondary-product formation. The degree of aggregate formation is influenced by the degree of mixing. Since the degree of mixing necessary to achieve equivalent oxygen transfer or equivalent shear changes upon scale-up, the degree of aggregation and productivity may change (see Fig. 13.5).

Mixing depends on a combination of sparging and mechanical agitation. Oversparging can be a problem for plant cell cultures. Even though photoautotrophic growth is not important in most cultures, elevated CO₂ levels can enhance productivity. Plants make at least one volatile hormone, ethylene, and its rapid removal can affect productivity. With plant cell cultures, optimizing the gas composition, sparging rate, and degree of mechanical agitation is a difficult problem.

The low growth rates of plant cells present other problems for large-scale systems. The primary problem is maintenance of aseptic conditions for the two to four weeks often necessary to complete a fermentation. Additionally, the low growth rates reduce volumetric productivities to levels that diminish the economic attractiveness of plant cell cultures.

A further problem is the apparent genetic instability of many cell lines. Often, suspension and callus cultures will produce a desired compound initially, but after three to six months the capacity to make the product often decreases considerably. This loss of productivity may be due to inadequate nutrition or may have a genetic or epigenetic basis. Artificial cell culture tends to select for cells with higher ploidy levels (tetraploid instead

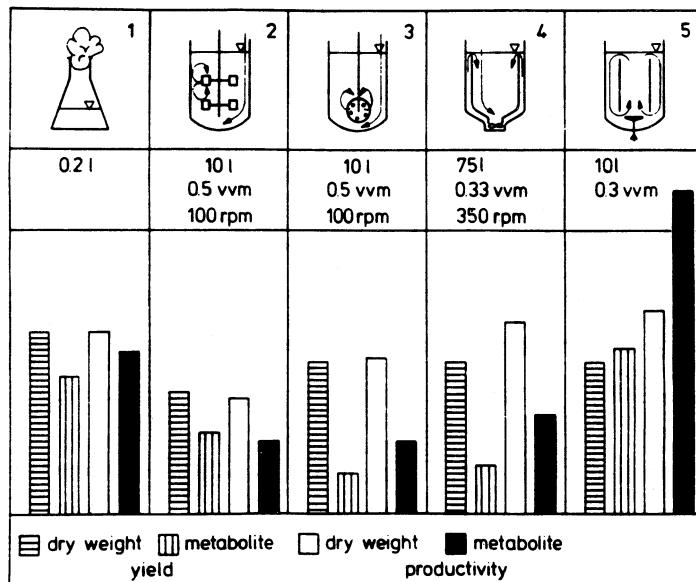


Figure 13.5. Comparison of yield (g/l, mmol/l) and productivity (g/l/day, mmol/l/day) for biomass (*Morinda citrifolia*) and anthraquinone in different culture systems: (1) shake flask; (2) flat-blade turbine; (3) perforated disc impeller; (4) draft tube reactor with Kaplan turbine; (5) airlift reactor. (With permission, from F. Wagner and H. Vogelmann in W. Barz, E. Reinhard, and M. H. Zenk, eds., *Plant Tissue Culture and Its Biotechnological Application*, Springer-Verlag, New York, 1977, p. 250.)