

CELL LINES FOR DRUG DISCOVERY AND DEVELOPMENT - A REVIEW

Anjali Sahu, Deepika Sahu, Monika Barsagade, Sarika Sahu, Sonia Singh, Rashmi Verma Vikas Kumar Sahu, Umashankar Nirmalkar*

Bharti College of Pharmacy, Chandkhuri, Bhilai, (C.G), 491221, India

Bharti Institute of Pharmacy, Pulgaon, Bhilai, (C. G), 491221, India

*Corresponding Author's E-mail: umashankar.pharmacology@gmail.com

ABSTRACT

Generally, cell culture, involves utilization of a suspension or a stationary media, which results in the development of cells in an outside atmosphere with suitable conditions. On the other hand, enzymatic action is employed to attain cells for culture, which is the mechanical disaggregation process that is mostly chosen given that the methods give a simpler and less distressing way of achieving cells. The technique involves the segmentation of a tissue into slighter pieces from which the splinted cells is then gathered. On the other hand, primary explants systems can be utilized to attain the cells. Though, this process is principally helpful for the disaggregation of lesser amounts of tissue. Therefore, with the application of animal cell culture methods the utilization of animals in scientific trials will be considerably diminished. The current review mainly focuses in giving a substitute to animal testing by developing cells in a plate and is a feasible means to substitute animals in research.

Key words: - Cell culture, primary explants, disaggregation, suspension, stationary media.

1. INTRODUCTION

Cell line is a cell culture refined from a solitary cell along with cells with a homogeneous genetic form. Cell culture depicts the laboratory development of cells obtained from plants or animals¹. It is the method through which cells are developed in regulated environment usually exterior their normal atmosphere. Later than the significant cells have been separated from alive tissue, they can afterwards be retained in vigilantly regulated environment². For every kind of cell, these circumstances differ however commonly consist of an appropriate container with a medium to facilitate the supply of vital nutrients, augmentation factors, hormones, as well as gases³. Furthermore, controls the physiochemical atmosphere (pH buffer, osmotic pressure, temperature). An artificial substrate or surface (monolayer culture) is necessary for the majority of cells while others are capable to be developed freely buoyant in culture medium (suspension culture)⁴.

Careful consideration is essential towards the escalation medium to make sure that cells are given the entire components they need to mature⁵. The wide-ranging method of cell culture has been utilized broadly ever since the early 1900s for exploration on tissue growth as well as advancement, virus biology, properties of cancer cells, learning related to aging, genetics as well as gene analysis. Furthermore, comprehensive cell culture method has been developed towards production of biopharmaceuticals in magnitudes an additional aspect of the extensive field of biotechnology⁶.



Fig.1. Cell culture in a particular tissue culture plate

2. TYPES OF TISSUE CULTURE

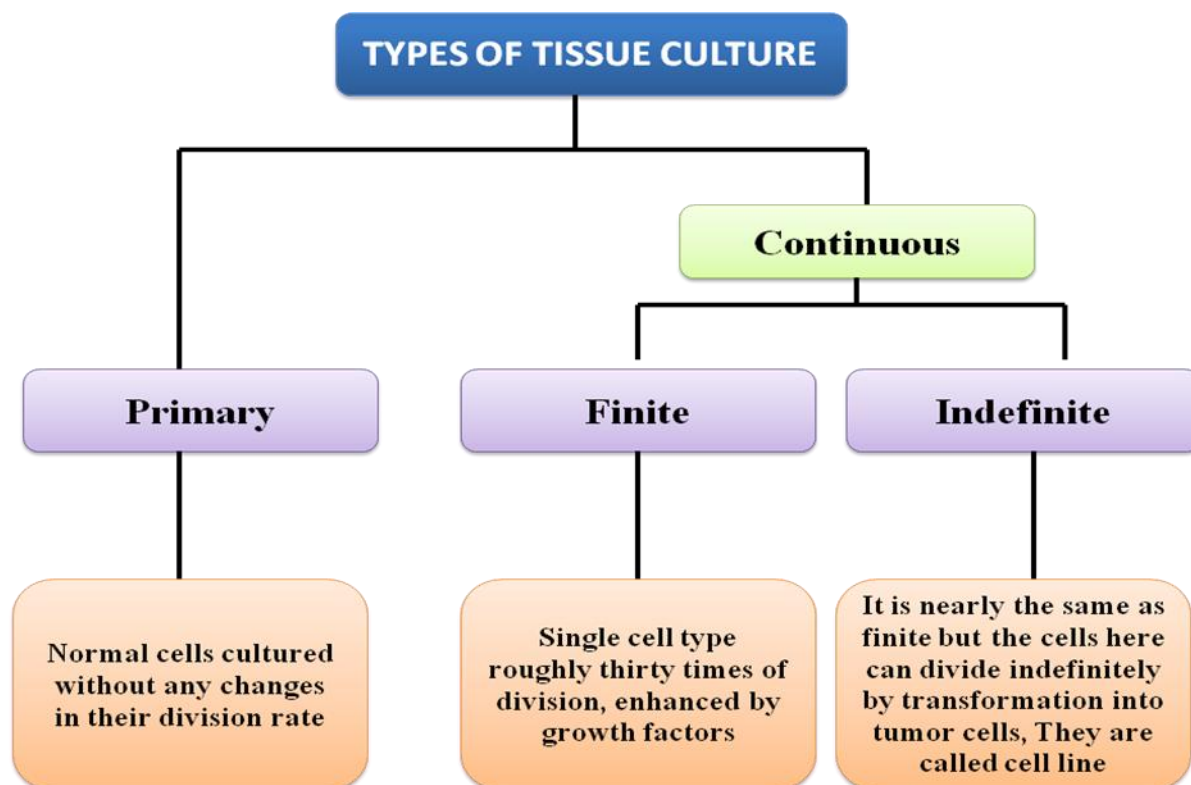


Fig.2. Tissue culture categorization

3. NOTIONS IN MAMMALIAN CELL CULTURE

3.1 Separation of cells:- Cells be able to separated from tissues for *ex vivo* culture in a number of means. They can be simply refined from blood; though merely the white cells are able to grow in culture⁷. The isolation of cells is done from firm tissues by absorbing the extracellular medium by means of enzymes like collagenase, trypsin, or pronase, prior to agitation of the tissue to discharge the cells into suspension. On the other hand, sections of tissue be sited in growth media, along with the cells that develop out are accessible for culture. This technique is called as explant culture⁸.

Primary cells are the cells that are cultured directly from a subject.



Fig.3. Primary cell separation

3.2 Maintaining cells in culture:- Cells are developed as well as retained on a suitable temperature and gas mixture (usually 37 °C, 5% CO₂ for mammalian cells) inside a cell incubator. For every cell type culture conditions differ broadly, and deviation of circumstances for a certain kind of cell can result in altered phenotypes⁹. The largely varied aspect in culture systems apart from temperature and gas mixture is the cell growth medium. The growth media formula can differ in pH, glucose concentration, growth factors, and the presence of other nutrients. For media supplementation, growth factors used are often derived from the serum of animal blood, such as fetal bovine serum (FBS), bovine calf serum, equine serum, and porcine serum¹⁰.



Fig.4. Cell culture medium

3.3 Components of cell culture media:-

- a) Carbon supply: Supply of energy¹¹.
- b) Amino acid: build up protein¹¹.
- c) Vitamins: encourage cell endurance & development¹¹.
- d) Balanced salt solution: An isotonic blend of ions for the maintenance of most favourable osmotic pressure inside the cells and to supply vital metal ions to work as cofactors for enzymatic response, cell bond etc¹¹.
- e) Phenol red dye: pH marker¹¹.
- f) Bicarbonate/HEPES buffer: To retain a fair pH in the media¹¹.

3.4 Manipulation of cultured cells:- Media changes, passaging cells, and transfecting cells are the general manipulations carried out on culture cells. These manipulations are usually carried out via tissue culture techniques that rely on aseptic system¹². Aseptic system aims in avoiding contamination with bacteria, yeast, or other cell lines. Manipulations are usually carried out within a biosafety cabinet or laminar flow cabinet in order to eliminate contaminating micro-organisms¹³. Antibiotics (e.g. penicillin and streptomycin) along with antifungals (e.g. amphotericin B) are also added to the growth

media. Acid is formed also the pH reduces as cells experience metabolic processes. Habitually, a pH indicator is added to the medium in order to quantify nutrient diminution¹⁴.



Fig.5. Laminar flow cabinet for inoculation of tissue culture¹⁴

4. ADVANTAGES OF ANIMAL CELL CULTURE

- Regulated physiochemical atmosphere (pH, temperature, osmotic pressure, O₂, etc.)¹⁵.
- Regulated and distinct physiological conditions¹⁵.
- Uniformity of cell types (attained throughout serial passages)¹⁵.
- Efficient, as slighter amounts of reagents are required than *in vivo*¹⁵.
- Lawful as well as fair queries of animal testing are avoided¹⁵.

5. DRAWBACKS OF ANIMAL CELL CULTURE

- The most complex part of cell culture is to retain the sterile aseptic condition¹⁶.
- In *in vitro* technique probabilities of chemical and microbial contamination is extremely high¹⁶.
- Skill is required so that performance of cells within culture be able to construe and synchronize¹⁶.
- For setting-up a cell culture facility the capital asset is extremely high¹⁶.

- In most of the cases the marker proteins do not express in sufficient measure under *in vitro* environment since, recognition of cell type is often complex¹⁶.

6. USES OF ANIMAL CELL CULTURE

- Toxicity Assessment** To study the consequences of novel drugs, cosmetics as well as chemicals on survival and growth in a large variety of cell types the cultured cells can be extensively employed alone or in combination with animal tests¹⁷.
- Cancer Investigation** As mutually ordinary cells as well as tumour cells can be developed within culture therefore; the fundamental dissimilarity among them can be intimately studied. Moreover, by the utilization of chemicals, viruses as well as radiation, it is feasible converting ordinary cultured cells to malignant cells. Hence, the method that cause the alteration can be deliberated. Cultured cancer cells in addition serves as a test method in determination of appropriate drugs as well as means for selectively destroying varieties of cancer¹⁸.
- Virology** Duplication of viruses within cell cultures (in place of animals) for use in vaccine production is one of the initial as well as chief utilization of cell culture. Cell cultures are furthermore extensively utilized in the experimental detection as well as separation of viruses, and basic research into how they develop and infect organisms¹⁹.
- Drug Screening & Development** Cell-based analyzation have turned out to be increasingly significant for the pharmaceutical industry, not just for cytotoxicity analysis however also for high throughput screening of compounds that may include possible use as drugs²⁰.

7. CONCLUSION

Cell culture is a potent method with the aim of leading important technical progresses that have optimistically impacted human wellbeing as well as lessened the quantity of animals in research. The object of employing fundamental replicas such as cells in investigation is creating as well as discovering strong, applicable & reproducible records so as to be utilized in identifying as well as in treatment of ailments that impact both humans and animals.

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