EXPERIMENT NO.: 5 **DATE:**

AIM: TYPES OF PRE-CLINICAL EXPERIMENTS: IN-VIVO, IN-VITRO, EX-VIVO, ETC

Introduction:

Drug Testing methods in pharmacology are traditionally called by their Latin names, such as in vivo, ex vivo, in vitro, in Silico and more.

1. The term in vivo refers to a type of experiment that is carried out within a whole, living organism, such as a plant or animal.
2. In vitro is exact opposite to in vivo. Instead experiment perform in living organisms studies or experiments conducted on microorganisms and cells outside of their normal biological environment whether that be in a test tube, culture dish, or so on.

   Common examples of in vitro experiments include

   - Cells derived from multicellular organisms (cell culture or tissue culture)
   - Subcellular components (e.g. mitochondria or ribosomes)
   - Cellular or subcellular extracts (e.g. wheat germ or reticulocyte extracts)
   - Purified molecules in the test tube (often proteins, DNA, or RNA, either individually or in combination).
3. Ex vivo procedures often involve living cells or tissues taken from an organism and cultured in a laboratory apparatus, usually under sterile conditions with no alterations for up to 24 hours. Experiments lasting longer than this using living cells or tissue are typically considered to be in vitro.
   - There is no major difference between in vitro and ex vivo preclinical study, In vitro means one which is performed outside the body, in the test tube withe the same natural conditions. Ex vitro means one which is performed outside the body with minimal alteration of the natural conditions.

   Examples of ex vivo models include:

   - Cardiovascular safety models using cardiac tissues or blood vessels
   - Inflammatory studies using skin biopsies
   - Isolated perfused heart models
4. In silico approaches are represented by techniques that use software to analyze data and often involve computational models or simulations based on existing information of closely related phenomena. The output can then be used to make predictions and suggest hypotheses as a basis for in vivo, ex vivo, and in vivo models

- The greatest advantage of in silico methods is that they are usually faster and cheaper than classical tests, whilst also reducing the number of animals to in vivo assays

Type of Study	In vivo	In vitro	Ex Vivo
Definition	Studies "within a living organism"	Study performed outside the body, in the test tube withe the same natural conditions	Study performed outside the body with minimal alteration of the natural conditions.
Cost	Very expensive	Relatively low cost	Very low cost
Time	Long and extensive	Relatively fast	Within 24 hrs
Example	Clinical trials and animal studies like local anesthetic effect on rabbit eye, pyrogen testing using rabbit.	Effect of various drug toxicity on vital organ of animal etc.	Common isolated organ experiment in laboratory like various drug effect on rat ileum, tracheal chain etc
Pros	More specific and reliable for observing biological effects in a test subject	Relative simplicity, species specificity, experimental control	Relative simplicity, species specificity, experimental control with minimum alteration of biological conditions
Cons	Strict regulations and compliance standards	Chances in alteration in result due to alteration in physiological conditions	Chances in alteration in result due to alteration in physiological conditions

Table 1: difference between In vivo, In vitro and Ex vivo model

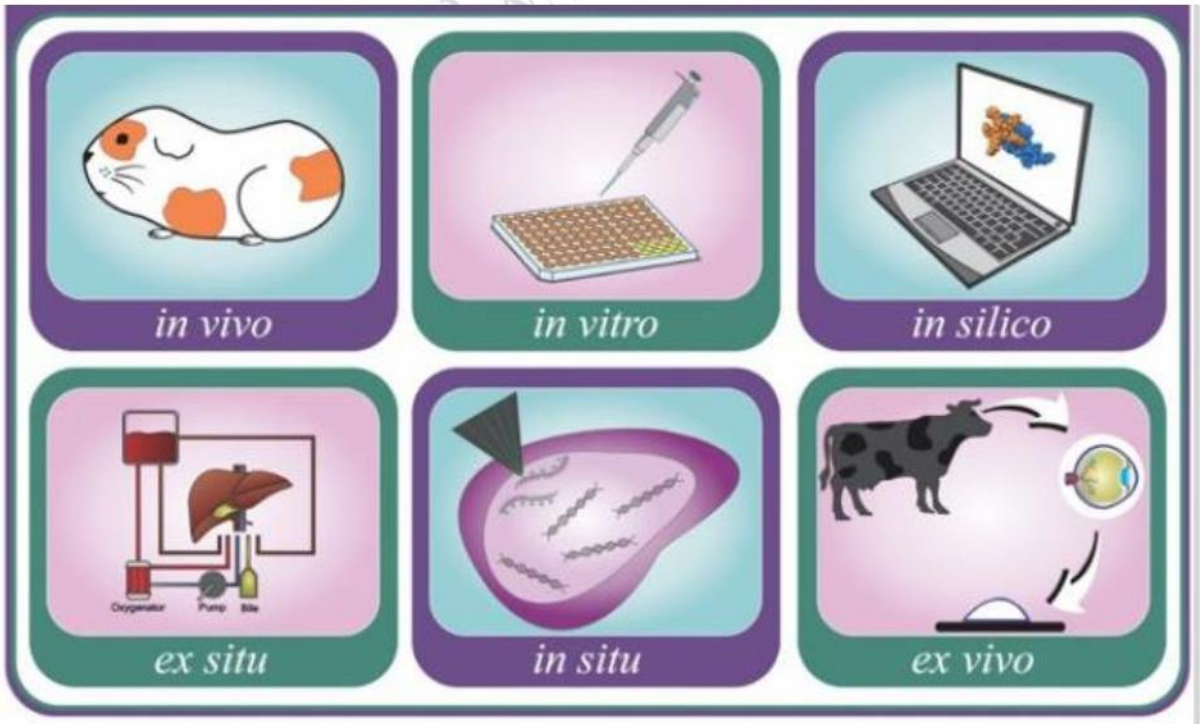

Figure 1: Sites for different preclinical model

Method	Application	Advantages	Limitations
In vitro techniques			
Conventional exposure (submersed)	High-throughput testing Initial screening for short-term effects	Controlled dosing Easy to perform Efficient use of material	Exposure of non- differentiated cells Non-physiological exposure No information on permeation No complex (multicellular) response No long-term exposure
ALI (monoculture) + Suspension exposure	Mechanistic uptake and toxicity studies	Controlled dosing Study of differentiated cells Efficient use of material	Non-physiological exposure No complex (multicellular) response No long-term exposure Advanced technology
ALI (monoculture) + Aerosol exposure chamber	Mechanistic uptake and toxicity studies Permeation studies	Relatively controlled dosing Study of differentiated cells Efficient use of material	No complex (multicellular) response No long-term exposure Complex exposure system Aerosol loss in the exposure system More complicated technology
ALI (mono/ co-culture) + Aerosol spraying	Mechanistic uptake and toxicity studies Permeation studies	Controlled cellular dose Study of differentiated cells Efficient use of material	No long-term exposure Potential shear stress of the cells More complicated technology
ALI (co-culture) + Aerosol exposure chamber	Absorption studies	Controlled dosing Efficient use of material Study on several cell types	Technically demanding No long-term exposure Aerosol loss in the exposure system Limited complex (multicellular) response
Ex-vivo techniques			
Isolated perfused lung	Absorption studies	Relatively controlled dosing Complex (multicellular) response Physiological exposure Efficient use of material	Technically demanding Short observation time
Precision-cut lung slices	Toxicity studies	Controlled cellular dose Complex (multicellular) response Efficient use of material	Non-physiological exposure Short observation time
In-vivo techniques			
Whole-body exposure	ADME studies Short-term/long-term, single exposure and multiple exposure	Physiological way of exposure No anesthesia or discomfort for animals Complex (multicellular) response	Large amount of material needed Dose not well defined

Table2: Types of animal model, their application, advantages and limitation

TEACHER'S SIGNATURE