KADI SARVA VISHWAVIDYALAYA
GANDHINAGAR

Ph.D. Course work for
Pharmaceutical sciences
2009-10

Course structure

Paper	Title	University Examination (marks)		Duration of exam	Schedule of exam
		Section A (general)	Section B (specialization)		
Paper-I	Research methodology	60	40	2 hrs	Every six months
Paper-II	Scientific communication	60	40	2 hrs	
Paper-III	(Recent Trends in Pharmaceutical Sciences)	100		2 hrs	

Detailed syllabus

Paper-I Research Methodology

Section-A (Common to all faculty) **60 marks**

1) Introduction to Research Methodology : Meaning of Research, Objectives of Research, Motivations in Research, Types of Research, Research Approaches, Significance of Research, Research Methods v/s Methodology, Research and Scientific Methods, Research Process, Criteria of Good Research 3

2) Defining the Research Problem : What is Research Problem?, Selecting the Problem, Necessity of and Techniques in defining the problem 6

3) Research Design: Meaning, Need, Features of Good Design, Concepts, Types. Basic Principles of Experimental Design, Developing a Research Plan 6

4) Sample Design : Implication, Steps. Criteria for selecting a sample procedure, Characteristics of Good sampling Procedure, Types of Sample Design, Selecting Random Samples, Complex random sampling Design. 7

5) Measurement and Scaling Techniques: Measurement in Research, Measurement Scales, Sources of Errors in measurement, Tests of Second measurement, Technique of developing Measurement Tools, Meaning of Scaling, Scale Classification Bases, Important Scaling Techniques, Scale Construction Techniques. 10

6) Methods of Data Collection: Collection of Primary Data, Observation Method, Interview method, Collection of Data through questionnaire and Schedules, Other methods. Collection of Secondary Data, Selection of appropriate method for data collection, Case Study Method, Guidelines for developing questionnaire, successful interviewing. Survey v/s experiment. 10

7) Processing and analysis of Data : Processing Operations (Meaning, Problems), Data Analysis (Elements), Statistics in Research, Measures of Central Tendency, Dispersion, Asymmetry, Relationship. Regression Analysis, Multiple correlation and Regression, Partial Correlation, Association in case of Attributes 10

8) Sampling Fundamentals : Definition, Need, Important sampling Distribution, Central limit theorem Sampling Theory, Sandler's A-test, Concept of Standard Error, Estimation, Estimating population mean, proportion. Sample size and its determination, Determination of sample size Based on i) Precision Rate and Confidence level ii) Bayesian Statistics. 12

9) Testing of Hypothesis: Meaning, Basic concepts, Flow diagram, Power of a hypothesis test, Important parametric tests, Hypothesis Testing of Means, Differences between Means, Comparing Two related samples, Testing of Proportion, Difference between proportions, Comparing variance to hypothesized population variance, Equality of variances of two normal populations, hypothesis testing of Correlation coefficients, Limitations of Tests of hypothesis. 12

10) Chi- square test : Applications, Steps, characteristics, limitations 3

11) Analysis of Variance and Covariance : Basic Principles, techniques, applications, Assumptions, limitations.

12) Analysis of Non-parametric or distribution-free Tests : Sign Test, Fisher-Irwin Test, McNemer Test, Wilcoxon Matched pair Test (Signed Rank Test), Rank 7

13) Sum Tests : a) Wilcoxon-Mann-Whitney Test b)Kruskal-Wallis Test, One sample Runs Test, Spearman's Rank Correlation, Kendall's Coefficient of Concordance, Multivariate Analysis Techniques: Characteristics, Application, Classification, Variables, Techniques, Factor Analysis (Methods, Rotation), Path Analysis. 7

Paper- I Research Methodology

SECTION-B (For Faculty of Pharmacy) 40 marks

1. **Pharmaceutics:**

Pharmaceutical Experimental Design: Factorial Designs, Fractional Factorial Designs, Rechtschaffner designs, D-optimal designs, Response surface methodology, Pharmaceutical process optimization and validation, Analyzing and minimizing variations in pharmaceuticals, Statistical experimental designs for formulations, Optimizing Formulations.

2. **Quality assurance**:

Development, validation, optimization of analytical methods based on HPLC, HPTLC, spectrophotometry, spectroflurometry, Gas chromatography etc., Quality assurance in pharmaceutical Industries, Contract Research Organizations etc.

Experimental design in the planning of syntheses, multivariate analysis of chemical and biological data, statistical validation of QSAR results.

3. **Pharmacology:**

Design and Statistical Analysis of experiments using laboratory animals, Sample size determinations in animal experiments, Controlling variability in animal experiments, Experimental designs for animal experimentations, Experimental methodology in Clinical Trials

4. **Pharmacognosy:**

Experimental Design in preparing and optimizing herbal formulations, testing herbs/herbal material on animals/ tissues/cells/humans.

Reference Books: Latest Editions of following Books

1) Kothari, C.R., Research Methodology (Methods and Techniques), New Age Publisher

2) Fundamentals of modern statistical methods By *Rand R. Wilcox*

3) Power Analysis for Experimental Research A Practical Guide for the Biological, Medical and Social Sciences by *R. Barker Bausell, Yu-Fang Li* Cambridge University Press

4) Design of Experiments: Statistical Principles of Research Design and Analysis, by *Robert O. Kuehl* Brooks/Cole

Research Methodology

Model Question Paper

Instructions : 1) Section-I is of 60 marks
2) Section-II is of 40 marks
3) There on negative marks for incorrect answers

Q1. Multiple Choice Questions. Choose one most correct answer from the provided choices. Write your choice on the right hand side column only. Illegibly written answers will not be considered. Each Question carries two marks.

i) Why is a control necessary in a well done experiment?
   a) To show what would normally happen and compare it with what happens when you change the independent variable.
   b) To keep the experiment from from becoming chaotic.
   c) So the experiment can be contained.
   d) For graphing purposes only

ii) Consider the following data:
   14; 16; 16; • 22; 25; 38; 38; 38; 38; 2000
   Which of the measures of central tendency would be the least useful?
   a) mean
   b) mode
   c) median

iii) As the degrees of freedom increase (and especially when the degrees of freedom are more than 90), the graph of the chi-square distribution looks more and more _____.
   a) symmetrical
   b) skewed right
   c) skewed left
   d) asymmetrical

iv) The Goodness-of-Fit hypothesis test is typically a _____.
   a) two-tailed test
   b) wagging-tailed test
   c) left-tailed test
   d) right-tailed test

v) Determine the sampling technique: A medical researcher does a random survey of 100 female doctors and 100 male doctors.
   a) stratified
   b) systematic

c) simple random
d) cluster

vi) Following is not the example of tests.
a) Chi test b) t-test c) pie test d) F-test

vii) Following is not the part of basic principles of experimental designs
a) Replication b) Randomization c) Local Control d) Reduction

viii) Following is the type of informal experimental designs.
a) Before-and after with control design
b) b) Completely randomized Design
c) Latin square Design
d) Factorial Designs

ix) For data that is normally distributed, is it possible for the standard deviation to be larger than the mean?
a) No.
b) Yes.
c) There is not enough information to determine.

x) What is the difference between the independent and dependent variables in an experiment?
A. The independent variable is quantitative and the dependent variable is not.
B. The independent variable is what is changed and the dependent variable is what is measured.
C. The independent variable has disowned his parents and the dependent variable still relies on them for food, shelter, and gas money.
D. The independent variable is graphed on the y-axis and the dependent is graphed on the x-axis.

Q2. Fill in the Blanks: (2 x 10 marks)

i) ---------- refers to a design that has more than one independent variable.
ii) ---------- is an external variable that affects the internal variable and intertwines with other extraneous variables such that it is difficult to determine unique effects of each.
iii) ---------- is the non-manipulated variable in factorial design.
iv) ---------- is an arbitrary value, designated as the significance level.
v) ---------- is the measure of the flat-toppedness of a distribution curve
vi) ---------- factorial designs consider the effect of varying two factors on the dependent variable.

vii) ---------- technique is used design or plan the experiment in such a way that thew variations caused by extraneous factors can all be combined under the general heading of “chance”.

viii) ---------- measures seperstely the relationship between two variables in such a way that the effects of other related variables are eliminated.

ix) ---------- defines the limits within which the parameters of the population are expected to lie with a specified degree of confidence.

x) When there really is a difference (association, correlation) overall, but random sampling caused your data to not show a statistically significant difference, the errors responsible for this are called _____

Q3. Answer true or false for the following statements: A correlation coefficient: (4 marks)

a. Should not be calculated when there is an underlying relationship between the two variables but it is not linear.
b. Does not provide evidence of a causal relationship between two variables.
c. Should not be used to judge the biological importance of the relationship between two variables.
d. Should be performed only when certain assumptions are satisfied (e.g. variables measured on a random sample of individuals, both the variables are quantitative and at least one of the two variables need to be normally distributed).

Q4. Answer true or false for the following statements: The paired t-test: (5 marks)

a. Tests the null hypothesis that the two population means are equal
b. Must have equally sized numbers of observations in each group.
c. Assumes that the data in each group are normally distributed.
d. Is appropriate for comparing the means of independent groups of observations.
e. When appropriately used, is more powerful when the sample size is large.

Q5. Answer true or false for the following statements (5 marks)

a. The p-value is the probability of the sample data arising by chance.
b. The p-value is an arbitrary value, designated as the significance level.
c. The p-value is the chance of getting an observed effect if the null hypothesis was false.
d. The p-value is the chance of getting an observed effect if the null hypothesis was true.
e. A very small p-value allows us to say that there is enough evidence to accept the null hypothesis.

Q6. Match the following :

A) Match the following examples with type of research design (5 marks)

Example	**Research Design**
i) Effect of digital BP instruments accuracy.	a) Exploratory Research studies.
ii) CVS Research in Institute during1990-1995)	b) Descriptive and Diagnostic Res. Studies.
iii) Effect of temp on productivity	c) Hypothesis Testing Research studies.
iv) Effect of fertilizer X on plant cultivation	
v) Effect of mobile users and brain tumor.	

Q7. Write the below functions in sequence. (e.g. d-a-c-b-f-e) (1 mark)

a) Selection of samples. b) Analysis of data c) Designing the methods of data collection. d) Formulating the objective of study e) Report preparation f) Collection data

SECTION-II **(Max. Marks -40)**

Design an experiment for any one of the under mentioned research topic:

I) To prove that chronic Aspirin administration promotes gastric ulceration in rats.

II) To prove that given HPLC method for determination of Ciprofloxacin in biological samples is more accurate, precise and reproducible than the UV spectrophotometric method.

III) To prepare and evaluate a tablet dosage form of Paracetamol using three excipients and optimum temperature and humidity condition to achieve the dissolution, disintegration and hardness parameters equivalent to that of a standard market formulation.

IV) You are given three herbal drug extracts which are reported to possess anti-inflammatory activity. Design an experiment to find out the optimum proportion of each of the extracts to be combined to achieve maximum therapeutic efficacy.

Note : The design should describe following :

a) Type of design (e.g. Cross-over, 2 x 2 factorial etc.) 3 marks
b) Sample size 2 marks
c) Design table/ Flow chart 15 marks
d) Parameters to be studied 3 marks
e) Sample Selection method 5 marks
f) Statistical Analysis to be involved in the study and the basis 12 marks

Paper-II Scientific Communication

Section A (Common for all faculty) **60 marks**

1. Basics of Communication skill.
2. English Grammar
   a) Word Choice, Sentence Structure, paragraph structure
3. Types of Scientific Communication.
4. Importance of publishing research paper
5. Publishing paper :
   a) Preliemnaries, Format, Choosing Journal
   b) Title, Running Title
   c) Authors: Single and Multi authorship
   d) Writing Abstract
   e) Selecting Keywords
   f) Introduction section
   g) Materials and Methods Section
   h) Result Section
   i) Figures : Design Principles, Legends, Table components, Graphs: Types, Style, Tables v/s Graph
   j) Discussion Section: Format, Grammar Style, Content.
   k) Acknowledgements
   l) References : Different Styles
   m) Communication with the Editor, Handling Referees' Comments, Galey Proofs
6. Writing Review Articles
7. Preparing and Delivering of Oral Presentation
8. Avoiding Plagiarism
9. Preparing documents for, MoUs, Confidentiality Agreements.
10. IUPAC symbols and Terminology for physicochemical quantities and Units, SI prefixes, Fundamental Constants, Standard Abbreviations and Symbols

Section B: **40 marks**

Pharmaceutical Sciences:

Exercises based on scientific writing skills in research publications relevant to Pharmaceutical Sciences.

Reference Books:

1) Study and Communication Skills for the Biosciences by *Stuart Johnson and Jon Scott,* Oxford University Press
2) Write and Publish a Scientific Paper by *Robert A. Day* Oryx Press
3) Scientific Easy when you know how by *Jennifer Peat* BMJ Books

4) Research Projects and Research Proposals A Guide for Scientists Seeking Funding by *Paul G. Chapin* Cambridge University Press

Model Question Paper for Paper-II (Scientific Writing)

1) Which of the following is the most correct title for the provided abstract? (4marks)
   a) Anti-staphylococcal activity and mode of action of clofazimine
   b) Bactericidal property of Clofazimine
   c) Cofazimine is effective against S.aureus

ABSTRACT

Objectives: Infections caused by Staphylococcus aureus might be treated with agents whose primary indications are for other infections. Clofazimine, an established anti-mycobacterial drug, could be such a candidate. However, the anti-staphylococcal properties of clofazimine have not been fully described and its mode of action, possibly involving inhibition of both RNA polymerase and a membrane-located target, has not been explored in detail. We have now conducted experiments to address these issues. Methods: Using established procedures, we examined the activity of clofazimine against a range of clinical isolates of S. aureus and determined whether it was bactericidal, exhibited a post-antibiotic effect (PAE), or interacted synergically with other agents. The potential for emergence of clofazimine-resistant mutants was also examined. Mode of action studies involved macromolecular synthesis assays, cross-screening against rifampicin-resistant mutants, susceptibility of RNA polymerase to clofazimine in vitro and several methods to detect drug-induced membrane damage. Results: Clofazimine demonstrated good anti-staphylococcal activity encompassing MSSA, MRSA and GISA. It was bactericidal and resistant mutants could not be isolated. Clofazimine did not exhibit a PAE and failed to act synergically with other drugs. No evidence for specific inhibition of RNA polymerase was obtained. Clofazimine caused non-specific inhibition of DNA, RNA and protein synthesis, consistent with membrane-damaging activity that was detected in three independent assays for membrane disrupting agents. Conclusions: Clofazimine is a potent anti-staphylococcal agent. It appears to be a membrane-disrupting agent and does not inhibit RNA polymerase.

2) Choose the correct word from the given choices to replace the underlined word/fill in the blank in the given sentences- (5 x 2 marks)
   a) Oral pediatric formulations of artemether are urgently needed, <u>however</u> the tablets are difficult to administer to young children, who cannot swallow whole tablets or tolerate the bitter taste of the crushed tablets.
      a. Because
      b. As
      c. Since
      d. however
   b) I _____ several eminent scholars in my study of herbal drug resources."
      i) Cited
      ii) Sited
   c) The differences between the control and experimental groups were _____
      i) Insignificant
      ii) Nonsignificant
   d) Noradrenaline _____ contractile response on rat vas deferens

i) elicit
ii) illicit

e) Resistance to antibiotics is becoming _____ difficult problem in the management of bacterial infections.

i) An Increasingly
ii) More
iii) Highly

Q 3. Answer in Short:

a) Give full form of IUPAC (2)
b) Enumerate three most commonly followed styles of referencing (3)
c) What is Running title? (2)
d) Differentiate between histogram and bar chart (2)
e) Define Plagiarism (2)
f) Enumerate components of a tabular representation of result data (2)
g) Give the standard abbreviations of : (3)
   I) mililiter
   II) hour
   III) minutes
h) Differentiate between research paper and review article (3)
i) Define " Rapid Communication" (2)
j) Differentiate Symposium, panel Discussion and Seminar (3)

Q4. True or False (If false provide the correct answer) (2 x 6)

I) Passive voice is the most suitable sentence arrangement for scientific communication
II) Discussion section of a research paper discusses only the results obtained in the study
III) The first author is always the one who is the research guide and last author is one who is major contributor in experimental work.
IV) The numbers mentioned in the result table can have any number of decimal points.
V) Introduction section consists of summary of literature survey conducted prior to the study.
VI) The tense used in result section is mostly present tense.

Section –II

Q1. Provide the following for the given paper:

a) Correct Title(not more than 50 letters) (5)

b) Most suitable Keywords (2)

c) Abstract (not more than 250 words) (10)

d) Headings, footnotes and Legends to figures and tables (5)

Q2. Describe the result section using the provided tables and charts. (8)

Q3. A) Write a paragraph (not more than 100 words) on “Current Status of Pharmaceutical Industries in Gujarat”.
Note : You should put stress on method of writing, grammar, flow of thoughts, conclusion. Accurate data are not required. (10)

Paper-III Recent Trends in Pharmaceutical Sciences
100 Marks

Introduction and Applications of following:

a) New Drug Development strategies (Definitions and basic principles only)
    i. Combinatorial Chemistry
    ii. QSAR/SAR
    iii. Physicochemical Evaluation
    iv. Drug bio-screening and evaluation (Preclinical and Clinical)
b) Basic principles and applications of following:
    i. Spectrophotometry
    ii. Chromatography
    iii. Dissolution testing
    iv. Rheometry
    v. ELISA
    vi. Extraction methods for Herbal Drugs.
c) Applications of Nanotechnology in Pharmaceutical Science

References:

1) Remington's Pharmaceutical Sciences –Latest Edition
2) Comprehensive Pharmacy Review by Leon Shargel and others–Latest Edition

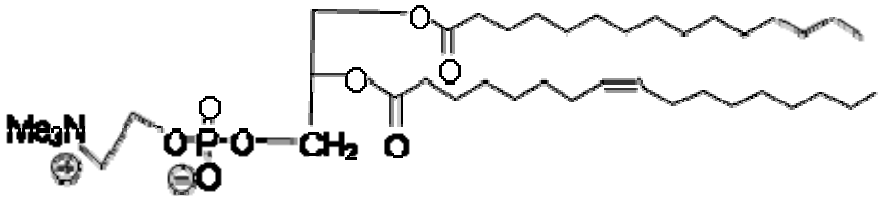
Model Question paper for PhD Coursework:

Paper-III Recent Trends in Pharmaceutical Sciences

Q1. Multiple Choice questions: **(20x 1.5 marks)**

1) Flame ionisation detector is used in _____ type of Chromatography method
    a) HPLC
    b) HPTLC
    c) Gas Chromatography
    d) Paper Chromatography
2) Wettability determination gives idea about
    a) Type of dosage form
    b) Type of packaging
    c) Type of buffer
    d) Type of manufacturing method.
3) Which of the following route of administration is fastest in making drug reach fastest in systemic circulation.
    a) Oral
    b) Intramuscular
    c) Intravenous
    d) Intraperitoneal
4) Effect of drug can vary due to :
    a) Age
    b) Body weight
    c) Disease State
    d) All of the above
5) Which of the following formulation provide longest duration of action
    a) Capsules
    b) Dispersible Tablets
    c) Sustained Relase Tablets
    d) Solution
    e) Suspension.

6) What type of molecule is the following structure?



a) A protein.
b) A nucleic acid.
c) A phospholipid.
d) A carbohydrate.

7) What is meant by a binding site?

a) The area of a macromolecular target that is occupied by a drug when it binds.
b) The portion of the drug to which a drug target binds.
c) The functional groups used by a drug in binding to a drug target.
d) The bonds involved in binding a drug to its target.

8) What does the symbol *P* represent in a QSAR equation?

a) pH
b) plasma concentration
c) partition coefficient
d) prodrug

9) Which of the following statements is false when comparing 3D QSAR with conventional QSAR?

a) Only drugs of the same structural class should be studied by 3D QSAR or QSAR.
b) 3D QSAR has a predictive quality unlike QSAR.
c) Experimental parameters are not required by 3D QSAR, but are for QSAR.
d) Results can be shown graphically in 3D QSAR, but not with QSAR.

10) Which of the following is NOT a laboratory safety rule?

a) You should never mix acids with bases
b) You should tie back your long hair
c) You should never add water to acid
d) All of the above are valid safety rules

11) What piece of laboratory equipment is best-suited for accurately measuring the volume of

a liquid?
a) graduated cylinder
b) beaker
c) Erlenmeyer flask
d) more than one of the above

12) Which piece of laboratory equipment can be used to store chemicals for long periods of time?
a) buret
b) evaporating dish
c) beaker
d) more than one of the above

13) The correct order for the basic features of a mass spectrometer is...
a) acceleration, deflection, detection, ionisation
b) ionisation, acceleration, deflection, detection
c) acceleration, ionisation, deflection, detection
d) acceleration, deflection, ionisation, detection

14) Which one of the following statements about ionisation in a mass spectrometer is incorrect?
a) gaseous atoms are ionised by bombarding them with high energy electrons
b) atoms are ionised so they can be accelerated
c) atoms are ionised so they can be deflected
d) it doesn't matter how much energy you use to ionise the atoms

15) Which one of the following pieces of information cannot be obtained from an infra-red spectrum?
a) the molecular mass
b) the presence of C=O bonds
c) the presence of O-H bonds
d) the identity of a compound through comparison with other spectra

16) The region of an infra-red spectrum where many absorptions take place is known as the...
a) thumbprint region
b) handprint region
c) footprint region

d) fingerprint region

17) Proton nmr is useful for investigating the structure of organic compounds because...

a) organic compounds contain carbon atoms
b) organic compounds are mostly covalent
c) hydrogen atoms are found in nearly all organic compounds
d) organic compounds have low boiling points

18) In the double beam spectrophotometer, the primary source of light is divided into two beams of

a. Equal intensity
b. Reference & sample intensity
c. Reference intensity
d. As per instrument

19) In HPTLC, _____ is used as support for stationary phase **:**

a. Silica
b. Aluminium sheet
c. Glass bead
d. Agarose

20) Which of the solvents is most polar

a) N-octane
b) N-hexane
c) Carbontetrachloride
d) methanol

Q2. Fill in the Blanks: (21 marks)

1) Middle IR range is _____.
2) Calibration Curve should obey _____ law.
3) Dissolution apparatus III is suitable for _____ dosage forms
4) Schedule ___ of Drugs and Cosmetics act refers to Drug Evaluation procedures
5) Angle of repose is used for determining _____ property of drugs and excipients.
6) _____ is widely used as a solvent for super critical fluid extraction
7) Total ash indicates the presence of _____ and _____ compounds
8) _____ and _____ extractive values are official in Indian herbal Pharmacopoeia.
9) HPTLC technique gives higher resolution than TLC techniques because of _____
10) Gas chromatography is not suitable for analysis of _____ type of compounds.

11) To work out the molecular mass of an organic molecule you would look at its _____spectra.
12) Most common side effect of NSAIDS is_____.
13) For antiseptic effect minimum ____ % alcohol can be used.
14) Distil water is free from_____ .
15) GCP means_____
16) Most common drug used during headache is _____.
17) _____and _____ are used most commonly during fever.

Q3. True/False (correct the false statement) (24 x 1.5 marks)

1) Dissolution limit for modified release form is not less than 90% release in specified time.
2) Emission wavelength is always greater than excitation wavelength in Fluorimetry.
3) In Phase-IV Clinical Trials premarketing surveillance is conducted
4) Increased Serum Creatinine levels refers to possibility of hepatic damage.
5) Crystalline form of drugs are faster absorbed than amorphous forms.
6) LAL test is for pyrogen testing in mice
7) Toxicity testing are normally done in G.pigs
8) CPCSEA permission will be is require for Animal house registration.
9) All experiments in human require Ethics Committee permission.
10) Placebo formulation does not contain any active drug molecule.
11) Sublingual medicaments are used to bypass First Pass Metabolism.
12) Antiemetic study evaluation can be done on rats.
13) Ex-vivo experiments include partly invitro experiments also.
14) Last British Pharmacopeia is BP-2010.
15) Control groups are not required for anti-inflammatory study.
16) Diclofenac of new formulation permission is banned.
17) Patent Act in INDIA is applicable.
18) 95% alcohol (Ethanol) means spirit.
19) Disprin is generic drug.
20) Synthetic wool is not source from animal.
21) We can drink “Water for injection”.
22) PPI- Proton Pump Inhibitors effects due to systemic effects.
23) All drugs have side effects.
24) Herbal drugs do not have Drug- drug interactions

Q4. Match the Following: **(13 marks)**

A)

Instrument	Principle
1.Cup and Bob Viscometer	a) Shear thinning
2.Cone and Plate Viscometer	b) Plastic Flow
3. Brookfield Viscometer	c) Thixotropy
4.Penetrometer	d) Shear thickening

B)

1) Volatile Oils	a) Super Critical Fluid Extractor
2) Extraction of Phytoconstituents	b) HPTLC technique
3) Finger Printing	c) Soxhlet Apparatus
4) Semi preparative Chromatography	d) Clavenger Apparatus

C)

1) Spectrophotometer	a) CNS activity
2) LAL Test	b) Absorbance
3) Photoactometer	c) Pyrogen Testing
4) Soxhlet assembly	d) Drug Extraction
5) Friability Testing	e) Tablets