रजिस्ट्री सं. डीएल (एन)-04/0007/2003--05 REGISTERED No. DL(N)—04/0007/2003—05

सत्यमेव जयते

भारत का राजपत्र
The Gazette of India

साप्ताहिक/WEEKLY

प्राधिकार से प्रकाशित

PUBLISHED BY AUTHORITY

सं॰ 19] नई दिल्ली, शनिवार, मई 10—मई 16, 2008 (वैशाख 20, 1930)

No. 19] NEW DELHI, SATURDAY, MAY 10—MAY 16, 2008 (VAISAKHA 20, 1930)

इस भाग में भिन्न पृष्ठ संख्या दी जाती है जिससे कि यह अलग संकलन के रूप में रखा जा सके।

(Separate paging is given to this Part in order that it may be filed as a separate compilation)

भाग III—खण्ड 4

[PART III—SECTION 4]

[सांविधिक निकायों द्वारा जारी की गई विविध अधिसूचनाएं जिसमें कि आदेश, विज्ञापन और सूचनाएं सम्मिलित हैं]

[Miscellaneous Notifications including Notifications, Orders, Advertisements and Notices issued by Statutory Bodies]

भारतीय रिज़र्व बैंक

मुंबई-400001, दिनांक 9 अप्रैल 2008

सदर्भ : बैंपविवि. सं. आईबीडी.-14241/23.13.048/2007-08--भारतीय रिज़र्व बैंक अधिनियम, 1934 (1934 का 2) की धारा 42 की उप-धारा (6) के खण्ड (ग) के अनुसरण में भारतीय रिज़र्व बैंक इसके द्वारा निदेश देता है कि उक्त अधिनियम की दूसरी अनुसूची में निम्नलिखित परिवर्तन किये जाएं :--

''अरब बांगलादेश बैंक लिमिटेड'' शब्दों के स्थान पर ''एबी बैंक लिमिटेड'' शब्द होंगे।

आनन्द सिन्हा

कार्यपालक निदेशक

[PUBLISHED IN THE GAZETTE OF INDIA, No.19, PART III, SECTION 4]

Ministry of Health and Family Welfare
(Pharmacy Council of India)

New Delhi, 10th May, 2008.

Pharm.D. Regulations 2008

Regulations framed under section 10 of the Pharmacy Act, 1948 (8 of 1948).

(As approved by the Government of India, Ministry of Health vide, letter No.V.13013/1/2007-PMS, dated the 13th March, 2008 and notified by the Pharmacy Council of India).

No.14-126/2007-PCI.— In exercise of the powers conferred by section 10 of the Pharmacy Act, 1948 (8 of 1948), the Pharmacy Council of India, with the approval of the Central Government, hereby makes the following regulations, namely:-

CHAPTER-I

1. Short title and commencement. – (1) These regulations may be called the Pharm.D. Regulations 2008.

   (2) They shall come into force from the date of their publication in the official Gazette.

2. Pharm.D. shall consist of a certificate, having passed the course of study and examination as prescribed in these regulations, for the purpose of registration as a pharmacist to practice the profession under the Pharmacy Act, 1948.

CHAPTER-II

3. Duration of the course. –

a) Pharm.D: The duration of the course shall be six academic years (five years of study and one year of internship or residency) full time with each academic year spread over a period of not less than two hundred working days. The period of six years duration is divided into two phases –

Phase I – consisting of First, Second, Third, Fourth and Fifth academic year.

Phase II – consisting of internship or residency training during sixth year involving posting in speciality units. It is a phase of training wherein a student is exposed to actual pharmacy practice or clinical pharmacy services and acquires skill under supervision so that he or she may become capable of functioning independently.

b) Pharm.D. (Post Baccalaureate): The duration of the course shall be for three academic years (two years of study and one year internship or residency) full time with each academic year spread over a period of not less than two hundred working days. The period of three years duration is divided into two phases –

Phase I – consisting of First and Second academic year.
Phase II – consisting of Internship or residency training during third year involving posting in speciality units. It is a phase of training wherein a student is exposed to actual pharmacy practice or clinical pharmacy services, and acquires skill under supervision so that he or she may become capable of functioning independently.

4. Minimum qualification for admission to. –

a) Pharm.D. Part-I Course – A pass in any of the following examinations -

(1) 10+2 examination with Physics and Chemistry as compulsory subjects along with one of the following subjects:

Mathematics or Biology.

(2) A pass in D.Pharm course from an institution approved by the Pharmacy Council of India under section 12 of the Pharmacy Act.

(3) Any other qualification approved by the Pharmacy Council of India as equivalent to any of the above examinations.

Provided that a student should complete the age of 17 years on or before 31st December of the year of admission to the course.

Provided that there shall be reservation of seats for the students belonging to the Scheduled Castes, Scheduled Tribes and other Backward Classes in accordance with the instructions issued by the Central Government/State Government/Union Territory Administration as the case may be from time to time.

b) Pharm.D. (Post Baccalaureate) Course -

A pass in B.Pharm from an institution approved by the Pharmacy Council of India under section 12 of the Pharmacy Act:

Provided that there shall be reservation of seats for the students belonging to the Scheduled Castes, Scheduled Tribes and other Backward Classes in accordance with the instructions issued by the Central Government/State Government/Union Territory Administration as the case may be from time to time.

5. Number of admissions in the above said programmes shall be as prescribed by the Pharmacy Council of India from time to time and presently be restricted as below –
   i) Pharm.D. Programme – 30 students.
   ii) Pharm.D. (Post Baccalaureate) Programme – 10 students.

6. Institutions running B.Pharm programme approved under section 12 of the Pharmacy Act, will only be permitted to run Pharm.D. programme. Pharm.D. (Post Baccalaureate) programme will be permitted only in those institutions which are permitted to run Pharm.D. programme.

7. Course of study. – The course of study for Pharm.D. shall include the subjects as given in the Tables below. The number of hours in a week, devoted to each subject for its teaching in theory, practical and tutorial shall not be less than that noted against it in columns (3), (4) and (5) below.

T A B L E S

First Year :

S.No.	Name of Subject	No. of hours of Theory	No. of hours of Practical	No. of hours of Tutorial
(1)	(2)	(3)	(4)	(5)
1.1	Human Anatomy and Physiology	3	3	1
1.2	Pharmaceutics	2	3	1
1.3	Medicinal Biochemistry	3	3	1
1.4	Pharmaceutical Organic Chemistry	3	3	1
1.5	Pharmaceutical Inorganic Chemistry	2	3	1
1.6	Remedial Mathematics/ Biology	3	3*	1
	Total hours	**16**	**18**	**6 = (40)**

* For Biology

Second Year:

S.No	Name of Subject	No. of hours of Theory	No. of hours of Practical	No. of hours of Tutorial
(1)	**(2)**	**(3)**	**(4)**	**(5)**
2.1	Pathophysiology	3	-	1
2.2	Pharmaceutical Microbiology	3	3	1
2.3	Pharmacognosy & Phytopharmaceuticals	3	3	1
2.4	Pharmacology-I	3	-	1
2.5	Community Pharmacy	2	-	1
2.6	Pharmacotherapeutics-I	3	3	1
	Total Hours	**17**	**9**	**6 = 32**

Third Year:

S.No.	Name of Subject	No. of hours of Theory	No. of hours of Practical	No. of hours of Tutorial
(1)	**(2)**	**(3)**	**(4)**	**(5)**
3.1	Pharmacology-II	3	3	1
3.2	Pharmaceutical Analysis	3	3	1
3.3	Pharmacotherapeutics-II	3	3	1
3.4	Pharmaceutical Jurisprudence	2	-	-
3.5	Medicinal Chemistry	3	3	1
3.6	Pharmaceutical Formulations	2	3	1
	Total hours	**16**	**15**	**5 = 36**

Fourth Year:

S.No.	Name of Subject	No. of hours of Theory	No. of hours of Practical/ Hospital Posting	No. of hours of Tutorial
(1)	**(2)**	**(3)**	**(4)**	**(5)**
4.1	Pharmacotherapeutics-III	3	3	1
4.2	Hospital Pharmacy	2	3	1
4.3	Clinical Pharmacy	3	3	1
4.4	Biostatistics & Research Methodology	2	-	1
4.5	Biopharmaceutics & Pharmacokinetics	3	3	1
4.6	Clinical Toxicology	2	-	1
	Total hours	**15**	**12**	**6 = 33**

Fifth Year:

S.No.	Name of Subject	No. of hours of Theory	No. of hours of Hospital posting*	No. of hours of Seminar
(1)	**(2)**	**(3)**	**(4)**	**(5)**
5.1	Clinical Research	3	-	1
5.2	Pharmacoepidemiology and Pharmacoeconomics	3	-	1
5.3	Clinical Pharmacokinetics & Pharmacotherapeutic Drug Monitoring	2	-	1
5.4	Clerkship *	-	-	1
5.5	Project work (Six Months)	-	20	-
	Total hours	**8**	**20**	**4 = 32**

***** Attending ward rounds on daily basis.

Sixth Year:

Internship or residency training including postings in speciality units. Student should independently provide the clinical pharmacy services to the allotted wards.

(i) Six months in General Medicine department, and

(ii) Two months each in three other speciality departments

8. Syllabus. – The syllabus for each subject of study in the said Tables shall be as specified in Appendix -A to these regulations.

9. Approval of the authority conducting the course of study. – (1) No person, institution, society or university shall start and conduct Pharm.D or Pharm.D. (Post Baccalaureate) programme without the prior approval of the Pharmacy Council of India.

(2) Any person or pharmacy college for the purpose of obtaining permission under sub-section (1) of section 12 of the Pharmacy Act, shall submit a scheme as prescribed by the Pharmacy Council of India.

(3) The scheme referred to in sub-regulation (2) above, shall be in such form and contain such particulars and be preferred in such manner and be accompanied with such fee as may be prescribed:

Provided that the Pharmacy Council of India shall not approve any institution under these regulations unless it provides adequate arrangements for teaching in regard to building, accommodation, labs., equipments, teaching staff, non-teaching staff, etc., as specified in Appendix-B to these regulations.

10. Examination. – (1) Every year there shall be an examination to examine the students.

(2) Each examination may be held twice every year. The first examination in a year shall be the annual examination and the second examination shall be supplementary examination.

(3) The examinations shall be of written and practical (including oral nature) carrying maximum marks for each part of a subject as indicated in Tables below :

T A B L E S

First Year examination :

S.No.	Name of Subject	Maximum marks for Theory			Maximum marks for Practicals		
		Examination	Sessional	Total	Examination	Sessional	Total
1.1	Human Anatomy and Physiology	70	30	100	70	30	100
1.2	Pharmaceutics	70	30	100	70	30	100
1.3	Medicinal Biochemistry	70	30	100	70	30	100
1.4	Pharmaceutical Organic Chemistry	70	30	100	70	30	100
1.5	Pharmaceutical Inorganic Chemistry	70	30	100	70	30	100
1.6	Remedial Mathematics/ Biology	70	30	100	70*	30*	100*
				600			600 = 1200

* for Biology.

Second Year examination :

S.No.	Name of Subject	Maximum marks for Theory			Maximum marks for Practicals		
		Examination	Sessional	Total	Examination	Sessional	Total
2.1	Pathophysiology	70	30	100	-	-	-
2.2	Pharmaceutical Microbiology	70	30	100	70	30	100
2.3	Pharmacognosy & Phytopharmaceuticals	70	30	100	70	30	100
2.4	Pharmacology-I	70	30	100	-	-	-
2.5	Community Pharmacy	70	30	100	-	-	-
2.6	Pharmacotherapeutics-I	70	30	100	70	30	100
				600			300 = 900

Third Year examination :

S.No.	Name of Subject	Maximum marks for Theory			Maximum marks for Practicals		
		Examination	Sessional	Total	Examination	Sessional	Total
3.1	Pharmacology-II	70	30	100	70	30	100
3.2	Pharmaceutical Analysis	70	30	100	70	30	100
3.3	Pharmacotherapeutics-II	70	30	100	70	30	100
3.4	Pharmaceutical Jurisprudence	70	30	100	-	-	-
3.5	Medicinal Chemistry	70	30	100	70	30	100
3.6	Pharmaceutical Formulations	70	30	100	70	30	100
				600			500 = 1100

Fourth Year examination :

S.No.	Name of Subject	Maximum marks for Theory			Maximum marks for Practicals		
		Examination	Sessional	Total	Examination	Sessional	Total
4.1	Pharmacotherapeutics-III	70	30	100	70	30	100
4.2	Hospital Pharmacy	70	30	100	70	30	100
4.3	Clinical Pharmacy	70	30	100	70	30	100
4.4	Biostatistics & Research Methodology	70	30	100	-	-	-
4.5	Biopharmaceutics & Pharmacokinetics	70	30	100	70	30	100
4.6	Clinical Toxicology	70	30	100	-	-	-
				600			400 = 1000

Fifth Year examination :

S.No.	Name of Subject	Maximum marks for Theory			Maximum marks for Practicals		
		Examination	Sessional	Total	Examination	Sessional	Total
5.1	Clinical Research	70	30	100	-	-	-
5.2	Pharmacoepidemiology and Pharmacoeconomics	70	30	100	-	-	-
5.3	Clinical Pharmacokinetics & Pharmacotherapeutic Drug Monitoring	70	30	100	-	-	-
5.4	Clerkship *	-	-	-	70	30	100
5.5	Project work (Six Months)	-	-	-	100**	-	100
				300			200 = 500

***** Attending ward rounds on daily basis.

****** 30 marks – viva-voce (oral)
70 marks – Thesis work

11. Eligibility for appearing Examination.— Only such students who produce certificate from the Head of the Institution in which he or she has undergone the Pharm.D. or as the case may be, the Pharm.D. (Post Baccalaureate) course, in proof of his or her having regularly and satisfactorily undergone the course of study by attending not less than 80% of the classes held both in theory and in practical separately in each subject shall be eligible for appearing at examination.

12. Mode of examinations.— (1) Theory examination shall be of three hours and practical examination shall be of four hours duration.

    (2) A Student who fails in theory or practical examination of a subject shall re-appear both in theory and practical of the same subject.

    (3) Practical examination shall also consist of a viva –voce (Oral) examination.

    (4) Clerkship examination – Oral examination shall be conducted after the completion of clerkship of students. An external and an internal examiner will evaluate the student. Students may be asked to present the allotted medical cases followed by discussion. Students' capabilities in delivering clinical pharmacy services, pharmaceutical care planning and knowledge of therapeutics shall be assessed.

13. Award of sessional marks and maintenance of records.— (1) A regular record of both theory and practical class work and examinations conducted in an institution imparting training for Pharm.D. or as the case may be, Pharm.D. (Post Baccalaureate) course, shall be maintained for each student in the institution and 30 marks for each theory and 30 marks for each practical subject shall be allotted as sessional.

    (2) There shall be at least two periodic sessional examinations during each academic year and the highest aggregate of any two performances shall form the basis of calculating sessional marks.

    (3) The sessional marks in practicals shall be allotted on the following basis:-

        (i) Actual performance in the sessional examination (20 marks);
        (ii) Day to day assessment in the practical class work, promptness, viva-voce record maintenance, etc. (10 marks).

14. Minimum marks for passing examination.— A student shall not be declared to have passed examination unless he or she secures at least 50% marks in each of the subjects separately in the theory examinations, including sessional marks and at least 50% marks in each of the practical examinations including sessional marks. The students securing 60% marks or above in aggregate in all subjects in a single attempt at the Pharm.D. or as the case may be, Pharm. D. (Post Baccalaureate) course examination shall be declared to have passed in first class. Students securing 75% marks or above in any subject or subjects shall be declared to have passed with distinction in the subject or those subjects provided he or she passes in all the subjects in a single attempt.

15. Eligibility for promotion to next year.— All students who have appeared for all the subjects and passed the first year annual examination are eligible for promotion to the second year and, so on. However, failure in more than two subjects shall debar him or her from promotion to the next year classes.

16. Internship.— (1) Internship is a phase of training wherein a student is expected to conduct actual practice of pharmacy and health care and acquires skills under the supervision so that he or she may become capable of functioning independently.

    (2) Every student has to undergo one year internship as per Appendix-C to these regulations.

17. Approval of examinations.— Examinations mentioned in regulations 10 to12 and 14 shall be held by the examining authority hereinafter referred to as the university, which shall be approved by the Pharmacy Council of India under sub-section (2) of section 12 of the Pharmacy Act, 1948. Such approval shall be granted only if the examining authority concerned fulfills the conditions as specified in Appendix–D to these regulations.

18. Certificate of passing examination.— Every student who has passed the examinations for the Pharm.D. (Doctor of Pharmacy) or Pharm.D. (Post Baccalaureate) (Doctor of Pharmacy) as the case may be, shall be granted a certificate by the examining authority.

CHAPTER-III
Practical training

19. Hospital posting.— Every student shall be posted in constituent hospital for a period of not less than fifty hours to be covered in not less than 200 working days in each of second, third & fourth year course. Each student shall submit report duly certified by the preceptor and duly attested by the Head of the Department or Institution as prescribed. In the fifth year, every student shall spend half a day in the morning hours attending ward rounds on daily basis as a part of clerkship. Theory teaching may be scheduled in the afternoon.

20. Project work.— (1) To allow the student to develop data collection and reporting skills in the area of community, hospital and clinical pharmacy, a project work shall be carried out under the supervision of a teacher. The project topic must be approved by the Head of the Department or Head of the Institution. The same shall be announced to students within one month of commencement of the fifth year classes. Project work shall be presented in a written report and as a seminar at the end of the year. External and the internal examiners shall do the assessment of the project work.

    (2) Project work shall comprise of objectives of the work, methodology, results, discussions and conclusions.

21. Objectives of project work.— The main objectives of the project work is to—

    (i) show the evidence of having made accurate description of published work of others and of having recorded the findings in an impartial manner; and

    (ii) develop the students in data collection, analysis and reporting and interpretation skills.

22. Methodology.— To complete the project work following methodology shall be adopted, namely:—

    (i) students shall work in groups of not less than *two* and not more than *four* under an authorised teacher;

    (ii) project topic shall be approved by the Head of the Department or Head of the Institution;

    (iii) project work chosen shall be related to the pharmacy practice in community, hospital and clinical setup. It shall be patient and treatment (Medicine) oriented, like drug utilisation reviews, pharmacoepidemiology, pharmacovigilance or pharmacoeconomics;

    (iv) project work shall be approved by the institutional ethics committee;

    (v) student shall present at least three seminars, one in the beginning, one at middle and one at the end of the project work; and

    (vi) two-page write-up of the project indicating title, objectives, methodology anticipated benefits and references shall be submitted to the Head of the Department or Head of the Institution.

23. Reporting .— (1) Student working on the project shall submit jointly to the Head of the Department or Head of the Institution a project report of about 40-50 pages. Project report should include a certificate issued by the authorised teacher, Head of the Department as well as by the Head of the Institution

(2) Project report shall be computer typed in double space using Times Roman font on A4 paper. The title shall be in bold with font size 18, sub-tiles in bold with font size 14 and the text with font size 12. The cover page of the project report shall contain details about the name of the student and the name of the authorised teacher with font size 14.

(3) Submission of the project report shall be done at least one month prior to the commencement of annual or supplementary examination.

24. Evaluation.— The following methodology shall be adopted for evaluating the project work—

(i) Project work shall be evaluated by internal and external examiners.

(ii) Students shall be evaluated in groups for four hours (i.e., about half an hour for a group of four students).

(iii) Three seminars presented by students shall be evaluated for twenty marks each and the average of best two shall be forwarded to the university with marks of other subjects.

(iv) Evaluation shall be done on the following items:

	Marks
a) Write up of the seminar	(7.5)
b) Presentation of work	(7.5)
c) Communication skills	(7.5)
d) Question and answer skills	(7.5)
Total	(30 marks)

(v) Final evaluation of project work shall be done on the following items:

	Marks
a) Write up of the seminar	(17.5)
b) Presentation of work	(17.5)
c) Communication skills	(17.5)
d) Question and answer skills	(17.5)
Total	(70 marks)

Explanation.— For the purposes of differentiation in the evaluation in case of topic being the same for the group of students, the same shall be done based on item numbers b, c and d mentioned above.

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Directorate of Academic & Planning

JAWAHARLAL NEHRU TECHNOLOGICAL UNIVERSITY KAKINADA
KAKINADA-533003, Andhra Pradesh, INDIA
(Established by AP Government Act No. 30 of 2008)

Lr. No. JNTUK/DAP/AC/Pharm.D/V Year/2019-20 *Date: 06-06-2019*

Dr. A. Mallikarjuna Prasad
M.E, Ph.D.,
Director, Academic Planning

To
All the Principals of Affiliated Colleges,
JNTUK, Kakinada

ACADEMIC CALENDAR FOR PHARM.D V YEAR (2015 BATCH)

V YEAR			
Description	**From**	**To**	**Weeks**
Commencement of Class Work	**10.06.2019**		
I Unit of Instructions	10.06.2019	31.08.2019	12W
I Mid Examinations	02.09.2019	07.09.2019	1W
II Unit of Instructions	09.09.2019	30.11.2019	12W
II Mid Examinations	02.12.2019	07.12.2019	1W
III Unit of Instructions	09.12.2019	29.02.2020	12W
III Mid Examinations	02.03.2020	07.03.2020	1W
Preparation & Practicals	09.03.2020	21.03.2020	2W
End Examinations	22.03.2020	04.04.2020	2W
Commencement of VI Year Class Work	**08.06.2020**		

Approved
Director Academic Planning

Copy to the Secretary to the Hon'ble Vice Chancellor, JNTUK.
Copy to PA to the Rector, JNTUK.
Copy to PA to the Registrar, JNTUK.
Copy to PA to the Director of Evaluation, JNTUK.

Vijaya Institute of Pharmaceutical Sciences for Women
ENIKEPADU VIJAYAWADA

PRINCIPAL
VIJAYA INSTITUTE
PHARMACEUTICAL SCIENCES FOR WOMEN
ENIKEPADU VIJAYAWADA 521 108

INSTITUTIONAL EXAMINATION COMMITTEE

VIJAYA INSTITUTE OFPHARMACEUTICAL SCIENCES FOR WOMEN
Enikepadu, Vijayawada – 521108

Date: 29-07-2019

OFFICE ORDER

INSTITUTIONAL EXAMINATION COMMITTEE

The Institutional Examination Committee for the academic year 2019 – 2020 is constituted as follows and it is effective for a period of 29-07-2019 to 21-12-2019. Following staff members are appointed as Institutional Examination Committee.

S.NO	NAME	DESIGNATION	POSITION	SIGNATURE
1	Dr. K. Padmalatha	Principal	Chairman	
2	Mr. S. Venkateswara Rao	Assoc. Professor	College Examination Officer	
3	Mrs. M. Vani	Assoc. Professor	Member	
4	Mrs. Ch. Anupama Swathi	Asst. Professor	Member	
5	Mr. Y. Naveen	Asst. Professor	Member	
6	Mrs. G. Pramoda	Asst. Professor	Member	

Functions and Responsibilities:

1. Ensure proper dissemination of information with regard to examination among all the stakeholders' viz. students / faculty / non – teaching staff / university authorities etc.
2. Receive and submission of exam notification / schedule from JNTUK web portal.
3. To ensure proper organization of in semester assessments / sessional / end semester examinations in the college.
4. Ensure proper communication with JNTUK with regards to examination and fulfillment of university circulars.
5. Appoint alternative external senior supervisor / chairman / internal examiners / external examiners for conduct of end semester theory / practical examination with permission of university authorities.
6. Record and issue the answer books and other exam related stationary to the invigilators / internal examiners 30 minutes before start the exam
7. Download and print the appropriate number of question papers at least 20 minutes before the commencement of the exam and maintaining absolute confidentiality
8. Resolve students / faculty / university grievances with regards to examinations.
9. Uploading internal theory / practical examination marks on JNTUK web portal.
10. Maintain records with regards to conduct of examination and results.

Copy to: 1. Establishment File
2. Concerned Faculty member

Dr. K. Padmalatha
PRINCIPAL
VIJAYA INSTITUTE OF
PHARMACEUTICAL SCIENCES FOR WOMEN
ENIKEPADU, VIJAYAWADA
PIN - 521 108

VIJAYA INSTITUTE OF PHARMACEUTICAL SCIENCES FOR WOMEN
ENIKEPADU, VIJAYAWADA – 521108.

Date: 29.08.2019

V PHARM D (R08) / I MID TIME TABLE

Date	Subject	Staff Name	Staff Signature
03.09.2019 (Tuesday)	Clinical Research	Mr. YN	
04.09.2019 (Wednesday)	Pharmacoepidemiology & Pharmacoeconomics	Mr.TS	
05.09.2019 (Thursday)	Clinical Pharmacokinetics & Pharmacotherapeutic Drug Monitoring	Dr.BD	

NOTE:

1. **Timings: 2.00pm to 4.00pm**
2. Send the Question Papers to Exam Section Mail. Id: vipwexams@gmail.com

Exams in charge
(Mr. S. Venkateswara Rao)
EXAMS-INCHARGE
VIJAYA INSTITUTE
PHARMACEUTICAL SCIENCES FOR WOMEN
ENIKEPADU, VIJAYAWADA 521 108

Principal
(Dr. K. Padmalatha)
VIJAYA INSTITUTE OF
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ENIKEPADU, VIJAYAWADA
PIN - 521 108

VIJAYA INSTITUTE OF PHARMACEUTICAL SCIENCES FOR WOMEN
ENIKEPADU, VIJAYAWADA – 521108.

Date: 23.11.2019

V PHARM D (R08) / II MID TIME TABLE

Date	Subject	Staff Signature
25.11.2019 (Monday)	Clinical Research	
26.11.2019 (Tuesday)	Pharmacoepidemiology & Pharmacoeconomics	
27.11.2019 (Wednesday)	Clinical Pharmacokinetics & Pharmacotherapeutic Drug Monitoring	

NOTE:

1. **Timings: 2.00pm to 4.00pm**
2. **Saturday : 11.00Am to 1.00 pm**
3. Send the Question Papers to Exam Section Mail. Id: vipwexams@gmail.com

Exams in charge
(Mr. S. Venkateswara Rao)
EXAMS-INCHARGE
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Vijaya Institute of Pharmaceutical Sciences for Women
Enikepadu, Vijayawada – 521108

Date: 27.02.2020

V Pharm. D / III Mid Exam Time Table

Date	Subject Name	Staff Name	Staff Signature
06.03.2020 (Friday)	Clinical Research (T5101)	Mr. Y. Naveen	
07.03.2020 (Saturday)	Pharmacoepidemiology and Pharmacoeconomics (T5102)	Mr. T. Sreenu	
09.03.2020 (Monday)	Clinical Pharmacokinetics & Pharmacotherapeutic Drug Monitoring (T5103)	Dr. B. Dhanush	

NOTE:

1. Timings: **01.30 PM – 03.30 PM**
2. Send the Question Papers to Exam Section Mail. Id: vipwexams@gmail.com

Principal
(Dr. K. Padmalatha)
VIJAYA INSTITUTE OF
PHARMACEUTICAL SCIENCES FOR WOMEN
ENIKEPADU, VIJAYAWADA

VIJAYA INSTITUTE OF PHARMACEUTICAL SCIENCES FOR WOMEN

ENIKEPADU, VIJAYAWADA - 521108

III, IV & V Pharm D MID EXAMS
STAFF INVIGILATION DUTIES

Time: 03.09.2019 - 09.09.2019 - 02 PM to 04 PM
07.09.2019 - 01 PM to 03 PM

DATE	III Ph.D		IV Ph.D		V Ph.D	
	Staff Name	Sign	Staff Name	Sign	Staff Name	Sign
03.09.2019	Mrs. Ch. Anupama Swathi		Mrs. Ch. Swathi		Dr. B. Dhanush	
04.09.2019	Mrs. Ch. Swathi		Dr. B. Dhanush		Dr. G. Manas Kumar	
05.09.2019	Dr. N. Prathibha		Dr. G. Manas Kumar		Mrs. Ch. Swathi	
06.09.2019	Dr. T. Sreenu		Mrs. Ch. Swathi			
07.09.2019	Dr. G. Manas Kumar		Dr. N. Prathibha			
09.09.2019	Dr. B. Dhanush		Dr. T. Sreenu			

Principal 30/8/19
(Dr. K. Padmalatha)

VIJAYA INSTITUTE OF
PHARMACEUTICAL SCIENCES FOR WOMEN
ENIKEPADU, VIJAYAWADA
PIN-521 108.

INTERNAL SQUAD COMMITTEE

VIJAYA INSTITUTE OFPHARMACEUTICAL SCIENCES FOR WOMEN
Enikepadu, Vijayawada – 521108

Date: 29-07-2019

OFFICE ORDER

INTERNAL SQUAD COMMITTEE

The Internal Squad Committee has been constructed for smooth conduct of sessional / end semester examinations for the academic year 2019 – 2020 for the period of 29-07-2019 to 21-12-2019. Following staff members are appointed as Internal Squad Committee.

S.NO	NAME	DESIGNATION	POSITION	SIGNATURE
1	Dr. K. Padmalatha	Principal	President	
2	Mr. S. Venkateswara Rao	Assoc. Professor	Chairman	
3	Mr. A. Jayarami Reddy	Asst. Professor	Member	
4	Dr. M. Tabitha Sharon	Asst. Professor	Member	
5	Mrs. G. Pramoda	Asst. Professor	Member	

Responsibilities:

1. Strict checking of unfair means is sole responsibility of members of committee.
2. Before the start of examination, the committee members should check every student.
3. Care should be taken by committee members, that the students should not carry mobile phones, calculator or any sort of electronic material inside the examination hall.
4. Check weather students are carrying hall tickets by committee members to maintain environment of examination. Any issue related to the unfair means should immediately report to the principal or college examination officer.

Copy to: 1. Establishment File
2. Concerned Faculty member

Dr.K. Padmalatha
PRINCIPAL
VIJAYA INSTITUTE OF
PHARMACEUTICAL SCIENCES FOR WOMEN
ENIKEPADU,VIJAYAWADA
PIN - 521 108

VIJAYA INSTITUTE OF PHARMACEUTICAL SCIENCES FOR WOMEN

ENIKAPDU,VIJAYAWADA-521108.

V PHARM. D / MID EXAMS
ATTENDANCE DIARY

Subject Name: Pharmacoepidemiology and Pharmacoeconomics

S.No	ROLL. No	STUDENT SIGNATURE		
		I MID	II MID	III MID
1	157N1T0002	- Ab -	B. Akhila Devi	B. Akhila Devi
2	157N1T0003	J.S.L.Priyanka	J.S.L.Priyanka	J.S.L.Priyanka
3	157N1T0004	V.L. Chaithra.	V.L. Chaithra	V.L. Chaithra
4	157N1T0005	- Vasavi	Vasavi-AK	AK. Vasavi
5	157N1T0006	- Ab -	ch. Sukanya.	ch. Sukanya
6	157N1T0007	B. Harshere.	B. Harsshere	B. Harsshere.
7	157N1T0008	K. Hema	K. Hema	K. Hema
8	157N1T0009	- Ab -	K. Madhuri	K. Madhuri
9	157N1T0010	M. Mounisha	M. Mounisha	M. Mounisha
10	157N1T0011	P. Thansi	P. Thansi	P. Thansi
11	157N1T0012	A. Ramya Sravanthi	A Ramya Sravanthi	A Ramya Sravanthi
12	157N1T0013	Y.S.N.S. Surya Akhila	Y.S.N.S. Surya Akhila	Y.S.N.S. Surya Akhila
13	157N1T0014	G. Bhargavi	G. Bhargavi	G. Bhargavi
14	157N1T0015	Sk Hafeezunnisa	Sk Hafeezunnisa	Sk Hafeezunnisa
15	157N1T0016	- Ab -	SK. Jareena	SK. Jareena
16	157N1T0017	Sk Danisha	Sk Danisha	Sk Danisha
17	157N1T0018	S. Sahitya	S. Sahitya	S. Sahitya
18	157N1T0019	M. Phani Mounika	M. Phani Mounika	M. Phani Mounika
19	157N1T0020	T. Sudeep Sainani	T. Sudeep Sainani	T. Sudeep Sainani
20	157N1T0021	T. Tejasvi Priyanka	T. Tejasvi Priyanka	T. Tejasvi Priyanka.
21	157N1T0022	- Ab -	E. Lavanya.	E. Lavanya
22	157N1T0023	K. Lavanya Rekha.	K. Lavanya Rekha.	K. Lavanya Rekha.
23	157N1T0024	Sindya	Sindya	Sindya
24	157N1T0025	M. Rajakumari	M. Rajakumari	M. Rajakumari
25	157N1T0026	M. Sivakshasi	M. Sivakshasi	M. Sivakshasi
26	157N1T0027	Absent	- Absent -	Absent
27	157N1T0028			
28	157N1T0029	Ch. Sai	Ch. Sai	Ch. Sai
29	15431T0009	K. Jyothirmayee	K. Jyothirmayee	K. Jyothirmayee
30	187N1T0101	- Ab -	P. Meghana.	P. Meghana.
31	187N1T0102	V.M. Mudlitha	V.M. Mudlitha	V.M. Mudlitha
Total Number of Students		29	30	31
Signature of Invigilator			N. Pratibha.	
Exams Incharge		S. Venkatesha	S. Venkatesha	S. Venkatesha
Signature of Head of the Institution				

VIJAYA INSTITUTE OF PHARMACEUTICAL SCIENCES FOR WOMEN

ENIKAPDU, VIJAYAWADA-521108.

V PHARM. D / MID EXAMS
ATTENDANCE DIARY

Subject Name: Clinical Research

S.No	ROLL. No	STUDENT SIGNATURE		
		I MID	II MID	III MID
1	157N1T0002	AB	B. Akhila Sri	B. Akhila Sri
2	157N1T0003	J.S.L.Priyanka	J.S.L.Priyanka	J.S.L.Priyanka
3	157N1T0004	V.V.Chaithra.	V.V.Chaithra.	V.V.Chaithra
4	157N1T0005	AB	A.K.Vasavi	A.K.Vasavi
5	157N1T0006	AB	ch.Sukanya.	ch.Sukanya.
6	157N1T0007	B.Harsshene	B Harsshene	B.Harsshene
7	157N1T0008	K.Hema	-Ab-	K.Hema
8	157N1T0009	K.Madhuri	Madhuri	K.Madhuri
9	157N1T0010	M.Mounisha	M.Mounisha	M.Mounisha
10	157N1T0011	P.Thansi	P.Thansi	P.Thansi
11	157N1T0012	A.Ramyasravanthi	A.Ramyasravanthi	A.Ramyasravanthi
12	157N1T0013	Y.S.N.S.Surya Akhila	Y.S.N.S.Surya Akhila	Y.S.N.S.Surya Akhila
13	157N1T0014	G.Bhargavi	G.Bhargavi	G.Bhargavi
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17	157N1T0018	S.Sahitya	S.Sahitya	—— Ab ——
18	157N1T0019	M.Phani Mounika	M.Phani Mounika	M.Phani Mounika
19	157N1T0020	T.Sudeepa Sainani	T.Sudeepa Sainani	T.Sudeepa Sainani
20	157N1T0021	T.Tejaswi Priyanka	T.Tejaswi Priyanka	T.Tejaswi Priyanka
21	157N1T0022	AB	E.Lavanya -	E.Lavanya
22	157N1T0023	K.Lavanyalekha	K.Lavanya Rekha	K.Lavanya Rekha.
23	157N1T0024	Sudeepa	Sudeepa	—— Ab ——
24	157N1T0025	AB	M.Rajakumari.	M.Rajakumari
25	157N1T0026	M.Sivakhari	M.Sivakhari	—— Ab ——
26	157N1T0027	Kishany	-Ab-	Kishany
27	157N1T0028	V.H.K.Gayathri	V.H.K.Gayathri	V.H.K.Gayathri
28	157N1T0029	Ch.Sai	Ch.Sai	Ch.Sai
29	15431T0009	K.Jyothimayee	-Ab-	K.Jyothimayee
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31	187N1T0102	AB	V.M.Mudiraj	V.M.Mudiraj
Total Number of Students		24	28	28
Signature of Invigilator		B.Dhanush		A.Bhavana
Exams Incharge		S.Venkateshwarlu	S.Venkateshwarlu	S.Venkateshwarlu
Signature of Head of the Institution				

VIJAYA INSTITUTE OF PHARMACEUTICAL SCIENCES FOR WOMEN
ENIKAPDU,VIJAYAWADA-521108.

V PHARM. D / MID EXAMS
ATTENDANCE DIARY

Subject Name: Clinical Pharmacokinetics and Pharmacotherapeutic Drug Monitoring

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		I MID	II MID	III MID
1	157N1T0002	– Ab –	B. Akhila Devi	B. Akhila Devi
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4	157N1T0005	A.K.Sri Vasavi	A.K.Sri Vasavi	Absent
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7	157N1T0008	K.Hema	K.Hema	K.Hema
8	157N1T0009	Madhuri.K	Madhuri.K	Absent
9	157N1T0010	M.Mounisha	M.Mounisha	M.Mounisha
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22	157N1T0023	K.LavanyaRekha.	K.LavanyaRekha	K.LavanyaRekha.
23	157N1T0024	Sindhya	Ab	Sindhya.
24	157N1T0025	– Ab –	M.Rajakumari.	M.Rajakumari
25	157N1T0026	– Ab –	M.Sivakshari	M.Sivakshari
26	157N1T0027	Krishnajyothi	Ab	Absent
27	157N1T0028	Gopala	Vkhargopal	Vkhargopal
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Exams Incharge		S.Venkateshwarlu	S.Venkateshwarlu	S.Venkateshwarlu
Signature of Head of the Institution				

Model of Evaluated Mid Exam

Answer Script

S.R.K. FOUNDATION'S

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ENIKEPADU, VIJAYAWADA

KNOWLEDGE IS POWER

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VIJAYAWADA

2019 - 2020

SESSIONAL BOOK

Name : V. L. Chaithra.

Class : Pharm-D - V year.

Roll No. : 157N1T0004.

Subject : Clinical pharmacokinetics and Therapeutic Drug Monitoring.

Internal	Objective	Subjective	Assignment	Total	Staff Sign	Student Sign
I		27		27		V.L. Chaithra
II		30		30		V.L. Chaithra
III		29		29		V.L. Chaithra

Final Average :

Staff Sign

HOD Sign

Date:- 05-09-2019

Mid Examinations -I

Clinical pharmacokinetics and Therapeutic Drug Monitoring.

18A7 @ Methods for designing drug dosage regimen:-

There are 4 types of methods for designing drug dosage regimen. They are:-

1. Individualised dosage regimen
2. Dosage regimen based on population average
3. Dosage regimen based on partial pharmacokinetic parameters
4. Empherical dosage regimen.

1. Individualised dosage regimen-

- This method is most accurate for designing a dosage regimen.
- It uses the pharmacokinetic parameters of drug in an individual patient based on plasma or serum concentrations of drug.
- The initial dose cannot be calculated but the dose adjustment can be done.
- Age, creatinine clearance, lean body mass are considered for designing this type of dosage regimen for a patient.

2. Dosage regimen based on population average:-

- The pharmacokinetic parameters (average) are taken into consideration for designing a dosage regimen. This is of two types - i. Fixed method/model ii. Adaptive model.

i) Fixed model:- The average pharmacokinetic parameters are calculated based on the previous published literature.

- The dose from the literature is calculated based on patient's age, weight etc.

ii) Adaptive model:- The dosage regimen is adapted based on the needs of the patient.

3) Dosage regimen based on partial pharmacokinetic parameters:-

- In some patients, the pharmacokinetic parameters cannot be measured or assessed.
- The pharmacist should monitor the dosage regimen based on patient's age, weight, drug characteristics etc.

4) Empirical dosage regimen:-

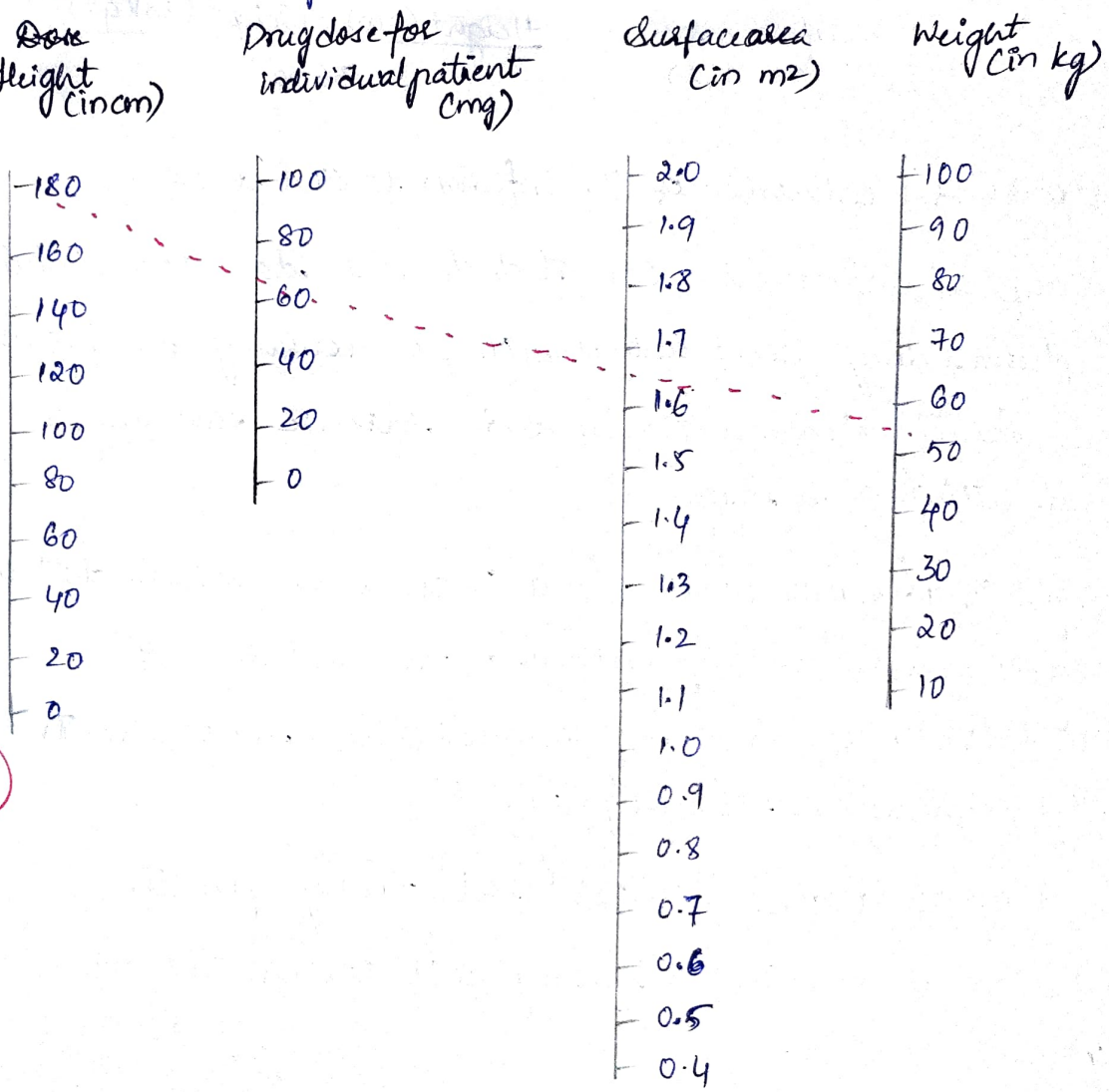
(Sometimes, the physician calculates the dose and dosage regimen without knowing the pharmacokinetic parameters of the patient.)

- The physician calculates the dose according to the patient, previous experience, observation and studies.

* Nomograms and Tabulations:-

The nomograms and tabulations are used to calculate the dose based on the patient's age, weight, body surface area

Example for a nomogram:-



4.3

Example for Tabulation:-

Tabulations are prepared majorly for narrow therapeutic index drugs like THEOPHYLLINE, for which the body fluids that to be measured are mentioned in case of monitoring drug concentrations.

Instead of a Nomogram ; Mosteller's formula can be used.

$$\text{Surface area } (m^2) = \frac{\text{Height (cm)} \times \text{Weight (in kgs)}}{3600}$$

(b) Guidelines for conversion of IV infusion to Oral dose :-

- Generally, IV infusion is converted to oral dose to maintain the plasma drug concentration without troubling the patient or to reduce economic burden and increase ease of administration of drugs.

- Example (IV) THEOPHYLLINE drug is used in patients to treat acute exacerbations in Asthma. The oral dose of THEOPHYLLINE is given immediately after the IV (Intravenous) dose is stopped.

- The drugs that are administered orally after IV infusion to maintain steady-state concentration, follows first (I) order kinetics.

- Two methods for calculating IV infusion to oral dose :-

* Method-I :- Assumes that the steady state concentration of drug after IV infusion is equal to the multiple dosing of drug.

$$C_{av}^{\infty} = \frac{S F D_0}{k V_d \tau}$$

where, C_{av}^{∞} = average concentration of drug

S = Salt form of drug.

k = constant F = Bioavailability

V_d = Volume of distribution

$\frac{D_0}{\tau}$ = Dosing rate

To calculate Dosing rate. $\boxed{\frac{D_0}{\tau} = \frac{C_{av}^{\infty} \cdot kV_d}{SF}}$

Example:- An adult male patient with asthma is been given with AMINOPHYLLINE drug through IV infusion at the rate of 34 mg/hour. Calculate the oral dose.

$$C_{av}^{\infty} = \frac{SF D_0}{kV_d \tau}$$

Aminophylline is salt form of Theophylline.

THEOPHYLLINE - 100% Bioavailability

AMINOPHYLLINE - 85% = 0.85

$S = 0.85$; $F = 1$; $\frac{D_0}{\tau}$ = 34 mg per 1 hour.

Dose of AMINOPHYLLINE per hour = $\frac{0.85 \times 1 \times 34}{1}$

= 28.9 mg/hour

Dose for 24 hours = 28.9×24

= 693.6 mg for 24 hours

∴ The oral dose of AMINOPHYLLINE for 24 hours = 693.6 mg

≈ 700 mg.

* Method-II :- Assumes that ~~the~~ IV dosing rate of a drug is equal

to Oral dosing.

Eg:- From the above example of AMINOPHYLLINE.

Dose for one hour = 34 mg

for 24 hours = 34 × 24

= 816 mg.

% dose rate = 816 × 0.85

= 693.6 mg

∴ Oral Dose of AMINOPHYLLINE for 24 hours = 693.6 mg

≈ 700 mg.

(5)

2.) IV dosing of a drug :- The IV dosing is calculated by 5 simultaneous steps.

* Step-1 :- Estimation of target steady state concentration.

$$C_{av}^{\infty} = \frac{C_{max}^{\infty} - C_{min}^{\infty}}{\ln(C_{max}^{\infty}/C_{min}^{\infty})}$$

where; C_{avg}^{∞} = average concentration of a drug.

C_{max}^{∞} = minimum toxic concentration

C_{min}^{∞} = (maximum) effective concentration.

Generally, the average of Cmax and Cmin are not calculated but the drugs that follow I order kinetics decline exponentially than to be declined in linear kinetics.

* Step-2:- Estimation of dosing rate to achieve average concentration.

$$\frac{D_0}{\tau} = \frac{Cl \cdot C_{avg}}{F}$$

$\frac{D_0}{\tau}$ = dosing rate

Cl = clearance of drug.

C_{avg} - average concentration of the drug

F - Bioavailability.

In IV (Intravenous) and systemic administration of drugs, bioavailability (F) is 1

$$\therefore \frac{D_0}{\tau} = Cl \cdot C_{avg}$$

* Step-3:- Estimation of maximum allowable τ.

The decline of plasma concentration from C_{max} to C_{min} is determined by Elimination half-life ($t_{1/2}$) and elimination rate constant (k_E).

So, the decline of C_{max} to C_{min} of plasma concentration can be identified.

$$C_{min}^{\infty} = C_{max}^{\infty} \cdot e^{k \tau_{max}}$$

To calculate τ_{max} :-

$$e^{k \tau_{max}} = \frac{C_{min}^{\infty}}{C_{max}^{\infty}}$$

$$\Rightarrow \boxed{T_{max} = \frac{\ln(C_{max}^{\infty} / C_{min}^{\infty})}{k}}$$

If the dose of the drug is not available the round it up to the nearest dose.

* Step - 4 :- Estimation of dose :-

(a) - If we know the dosing rate and dosage interval then we can calculate the dose as

Dose = Dosing rate x dosage interval.

- If the calculated dose is not available, the nearest dose can be given.
- To calculate the practical values of C_{max}^{∞} and C_{min}^{∞}, we have to calculate first dose of C_{max}^{∞} and C_{min}^{∞}.

$$C_{max}^{1^{st}\,dose} = \frac{Dose}{V_d}$$

where - V_d = volume of distribution

$$\therefore \boxed{C_{max}^{\infty} = C_{max}^{1^{st}\,dose} \cdot e^{-kT}}$$

(b) If we know the accumulation factor (R), then

$$R = \frac{1}{1 - e^{-kT}}$$

$$\therefore \boxed{C_{min}^{\infty} = C_{min}^{1^{st}\,dose} \times R}$$

* Step-5 :- Calculation of loading dose (D_L) (if needed) :-

- In some cases, the loading dose should be calculated for drugs having long half-lives ($t_{1/2}$) and immediate action is needed for the patient.

- Loading dose can be calculated as-

Loading dose (D_L) = maintenance dose (D_M) × C_{max}^{∞}.

$$D_L = D_M \cdot C_{max}^{\infty}$$

Loading dose can also be calculated as

$$D_L = C_{max}^{\infty} \times V_d .$$

→ Constant IV infusion :-

Step-1 :- Calculation of Infusion rate constant :-

The Infusion rate constant (R_0) can be calculated as

R_0 = clearance × steady state concentration

$$\Rightarrow \boxed{R_0 = Cl \cdot C_{ss}}$$

Step-2 :- Calculation of loading dose :-

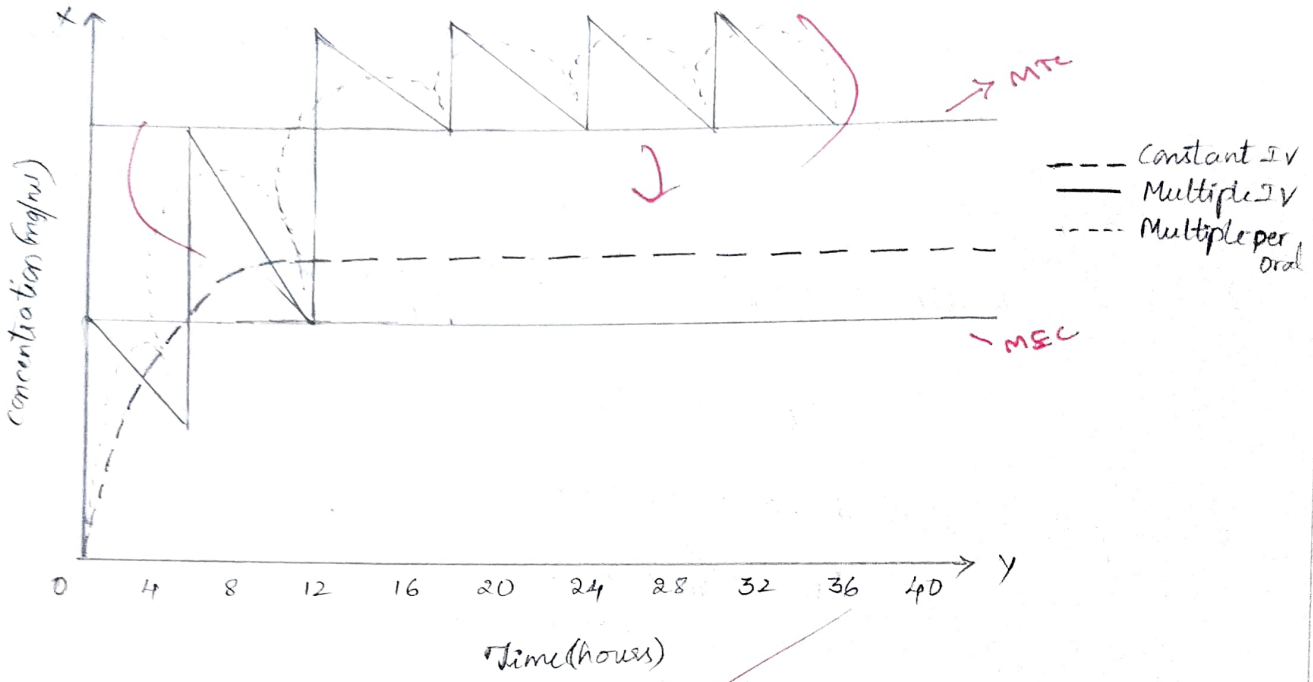
Loading dose $D_L = C_{ss} \cdot V_d$.

Where; C_{ss} - steady state concentration

V_d - volume of distribution.

→ Constant IV infusion

Heading



8½

If 250mg of dose of a drug is administered to a patient for every 6 hours. Then 40 mg/hour is the infusion rate.

---

39) Peak plasma concentration :- The concentration of drug at which maximum concentration is present in plasma is called peak plasma concentration. It is denoted by 'Cp'.

The units are mg/ml.

At this concentration the rate of absorption (Ka) is greater than rate of elimination (K_E).

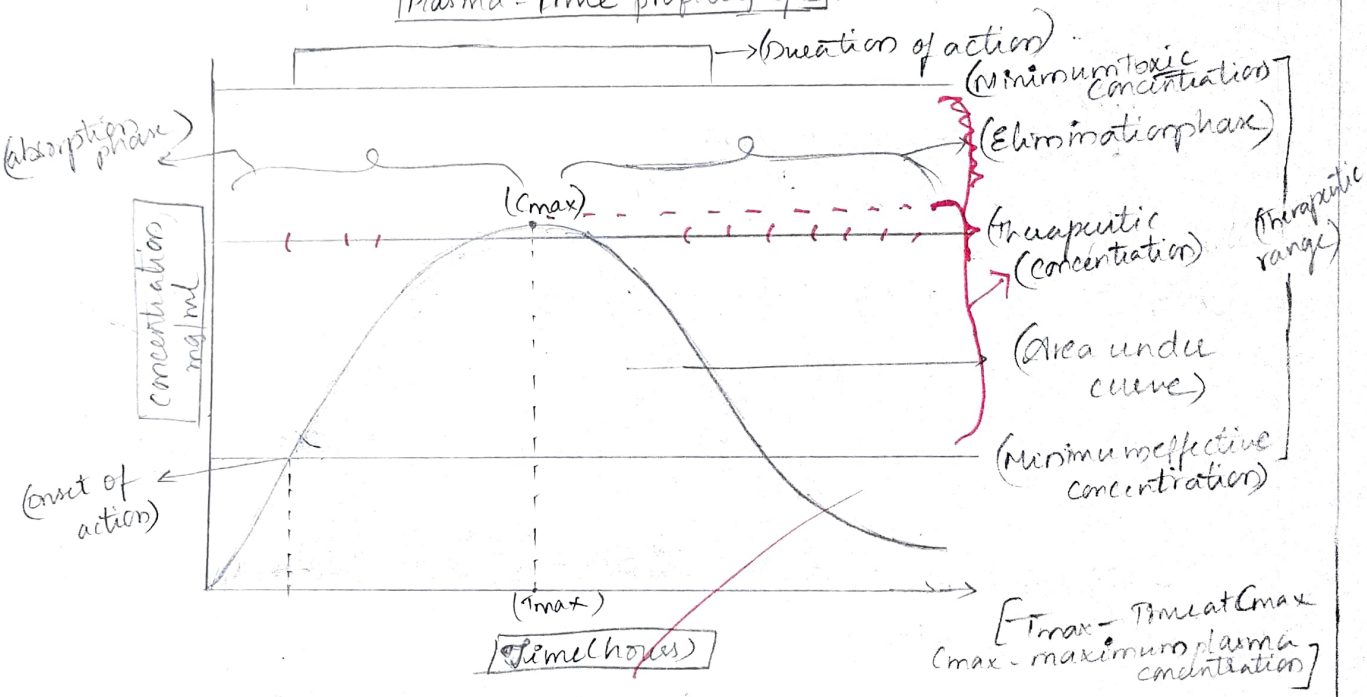
Area under curve (AUC) :- The maximum allowable area of plasma time profile curve at which the drug determines

bioavailability. The curve between absorption and elimination of drug from the body. It is denoted as 'AUC' (short terms).

Unit - µg/ml × hrs.

Therapeutic ranges - The range or extent between Minimum effective Concentration and maximum safe concentration or minimum toxic concentration is known as therapeutic range.

Plasma - Time profile graph



Above the minimum toxic concentration, it is toxic range and below the minimum effective concentration, it is sub-therapeutic range of a drug.

Onset of action :- The time at which there is initiation of effect of drug in the body is known as onset of action.

MEC (Minimum Effective concentration) :- The minimum concentration of the drug at which the therapeutic effect/action can be elicited.

Minimum Toxic Concentration(MTC):- Minimum Toxic concentration is also known as Maximum safe concentration (MSC). It is the concentration at which maximum effect of drug is seen in the body.

* Factors affecting Paediatric dosing:-

- The factors affecting pediatric dosing of a drug are:-
  (a) Age
  (b) Dose
  (c) Dosing frequency and
  (d) Route of administration.

(a) Age:- The drug clearance is affected or changed based on the age of a patient.

- Neonates have low clearance when compared to the infants.
- Children have less clearance of drug when compared to the adults.
- The skin is more permeable in case of pediatrics. So the Intramuscular route of administration is not a preferred route as it can be painful to the patient.

(b) Dose:- The dose of the paediatrics should be adjusted or calculated based on body weight (kgs), surface area (in m^2) and adult dose.

- Body surface area (BSA) = $\frac{\text{Height (in cm)} \times \text{weight (in kgs)}}{3600}$

∴ Child dose = $\frac{BSA}{1.73}$ × Adult dose.

- Dugs berger rule :-

Child's (approximate) appropriate dose = (1.5 × weight (in kgs) + 10) adult dose

- Clarck's rule :-

Child's appropriate dose = $\frac{\text{weight (in pounds (lbs))}}{150}$ × adult dose

- Total body weight = $\frac{\text{height (in cm)} * \text{weight (in kgs)}}{1.75}$ × 1

- Total body weight = $\frac{\text{height (in cm)} \times 1.75}{1000}$.

- If the calculated dose is above the adult dose then the adult dose should be given.

- Child dose based on age and adult dose :-

Neonates	-	12.5% of adult dose
1 month	-	14.5% of adult dose
3 months	-	18% of adult dose
5 months	-	22% of adult dose
7 months	-	25% of adult dose
1 year	-	33% of adult dose
3 years	-	40% of adult dose
5 years	-	50% of adult dose
7 years	-	60% of adult dose
12 years	-	75% of adult dose

- The drug clearance should be monitored based on dose given.

(c) Dosing frequency :- The dosing frequency should be decreased wherever necessary.

- The dosing interval and frequency should be maintained.

(d) Route of administration :-

(i) Oral :- The most preferred route of administration in pediatrics is oral route.

- If there is no alternative or indication then other routes of administration can be professed.

- The oral liquids are preferred. In case of chronic usage of oral liquids, the sugar-free preparations should be given to avoid tooth problems or dental problems and tooth decay.

- If the dose is minute i.e., <5ml, then dilute with water or milk (if no known interaction) and then administer to the patient.

- The teaspoon, tablespoon should not be used for measuring.

- The strength of the preparation should be used. Do not administer the medications with food.

(ii) Rectal route :- This is not professed route as the absorption is erratic.

(iii) Topical route :- The absorption is significant at different sites of the body.

- The topical route can be preferred as there is significant absorption.
- When prescribing the topical lotions, ointments and creams caution should be taken for hypersensitivity reactions.
- Topical usage of antibiotics should be avoided to prevent hypersensitivity.

iv) Parentral route:- This is not most preferred route unless until the indication is present.

- The Intramuscular administration should be avoided as it is painful.
- The Intravenous (IV) and Intramuscular (IM) administration should be done with caution.
- If there is need for parentral route then the assistance is needed to hold the patient.
- There should be maintenance of asceptic conditions. The needle sterilised with alcohol should become dry before usage.
- The pediatric needle should be used.
- If IM preparations should be given then prefer anterior part of thigh region.
- The syringe (needle) preparation and loading must be done at out of sight of patient.

- If intradermal administration is available, then prefer that route instead of Intravenous or Intramuscular route.

(9) - The use of same point of injection site should be avoided. Use multiple sites of administration if multiple doses are needed or administer through cannula (IV) if present or available.

27/30

Dh 06/09/19.

27/11/2019
Wednesday

Mid Examinations - II

1A) **Therapeutic drug monitoring :-**

Clinical laboratory measurements of chemical parameters with appropriate measurements or clinical interpretations that will directly influence the prescribing procedures is called as Therapeutic drug monitoring. (TDM)

Goal :- The main goal of TDM is to provide individualised dosage regimen.

established drugs for TDM :-

i) Cardioactive drugs - eg :- DIGOXIN, DIGITOXIN, NITRATES.
ii) Antidepressants - eg :- AMITRYPTILINE, NORTRIPTYLINE
iii) Benzodiazepines - eg :- DIAZEPAM, LORAZEPAM, NITRAZEPAM
iv) Antibiotics - eg :- Aminoglycosides, Tetracyclines
v) Chemotherapeutic agents - eg :- CISPLATIN, CYCLOPHOSPHAMIDE
vi) Immunosuppressants - eg :- Corticosteroids (PRENISOLONE)
vii) Bronchodilators - eg :- THEOPHYLLINE.

- The concentration of Theophylline drug at steady state concentration is 20-40 µg/ml.
- But the therapeutic effect and serious adverse drug reactions (ADRs) can also occur below 20µg/ml concentration.
- The TDM changes for every patient based on dose and dosage regimen.
- TDM explains the relation between serum drug concentration and drug response and serum drug concentration and Adverse drug reactions

- Some drugs are biomarkers for the specific disease condition, so during TDM those biomarkers can be measured without measuring concentration of drug in body fluids.

eg:- * Fasting blood sugar (FBS), Post prandial blood sugar (PPBS), Random blood Sugar (RBS) values are biomarkers for hypoglycemic drugs in diabetes mellitus.

* INR (International Normalised Ratio) values, clotting time are biomarkers when WARFARIN is administered.

Steps involved in Therapeutic Drug Monitoring (TDM):-

Select a drug

↓

Design a dosage regimen for the drug and prescribe to the patient

↓

Evaluate the patient response

↓

Determine the need for measuring serum drug concentrations

↓

Assay of drug concentration in body fluids

↓

Evaluation of pharmacokinetic parameters of the given drug

↓

Re-adjust the dosage regimen

↓

Evaluate the serum concentration levels

↓

↓

Counsel the patient for reactions of drug prescribed with other drugs (OTC drugs), herbal products etc.

Indications for Therapeutic Drug monitoring (TDM) :-

1. Toxic response.
2. Lack of therapeutic response.
3. Changes in patient and drug compliance.
4. Chronic diseases (chronic therapy)
5. Changes in drug therapy regimen.
6. Potential drug-drug interactions, adverse drug reactions and other effects due to polypharmacy.
7. Pharmacokinetic variability - eg :- ASPIRIN, DIGOXIN
8. Narrow therapeutic index drugs - eg :- DIGOXIN
9. Interindividual variation in metabolism - eg :- ASPIRIN
10. Changes in concentration due to renal and hepatic diseases
    eg :- Aminoglycosides, phenacetin.

Directions for drawing a sample :-

- The sample should be collected when the drug attains the steady state concentration.
- Centrifuge the sample collected to separate the plasma and serum, as the lag can lead to clotting of blood.
- Fresh sample should be taken. Use of anticoagulant can cause leak of anticoagulant into plasma or serum which gives negatives or false results.

- The samples should be stored in plastic cryovial tubes. The temperature should be maintained in the analytical area so as to avoid the clotting of sample (at high temperatures).

Timing of sample withdrawl:-

- The sample should be drawn during the trough phase or pre-dose phase (before administration of 2nd dose) to calculate the steady state concentration and avoid toxic concentration

- In case of Antibiotics, the sample is withdrawn at peak plasma concentration to evaluate maximum inhibitory concentration of drug. eg:- Aminoglycosides, Tetracyclines

- The effectiveness, pharmacokinetics of the drug should be known prior the process of TDM.

  eg:- DIGOXIN - the sample must be withdrawn after 6hours of administration of drug.

- If short half life drugs are considered then one sample is enough, but 3 samples are ideal to evaluate Cmax and Cmin ie., high and low concentrations of drug and after first dose random samples should be taken.

- If long half life drugs are considered, one sample is ideal. In case of alterations in absorption, renal clearance, then multiple samples can be collected.

  eg - CYCLOSPORINE - OD - sample collected ~~for 2-3~~ hours after administration.

PHENYTOIN - single sample (long half life)

CARBAMAZEPINE - half life - 48 hours
so sample collected after 3 hours of administration

LITHIUM - after 12 hours of sample administration.

DIGOXIN - after 6 hours of administration of drug, sample is collected

THEOPHYLLINE - conventional / controlled release - at any time
sustained release - 2-3 hours of drug administration

GENTAMICIN - IV - ½ hour
IM - 1 hour

$$\text{New dose} = \text{Old dose} * \frac{\text{desired concentration}}{\text{measured concentration}}$$

* Factors affecting, if the concentration is more than the anticipated values -
  - Error in ~~toxic~~ response
  - Increased bioavailability of drug
  - Increased protein binding of drug
  - Decreased elimination of drug
  - Decreased renal and hepatic clearance of drug.

* If the concentration estimated is less than anticipated values -
  - Error in toxic response
  - Error in collection of (timing) ~~of~~ sample
  - Decreased bioavailability of drug.
  - Altered renal and hepatic clearance of drug.

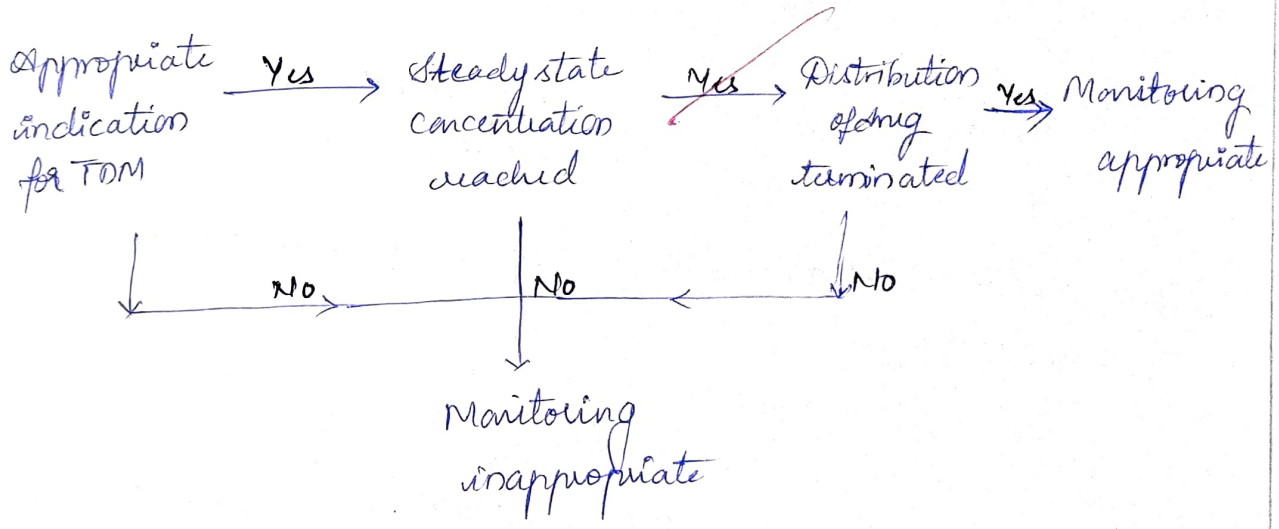
10

- Decreased protein binding of drug.

20.) Therapeutic drug monitoring of drugs used in seizures, organ transplantation, CVS diseases, psychiatric disorders :-

- Clinical laboratory measurements of chemical parameters with appropriate measurements or medical interpretations that will directly influence the prescribing procedures of a drug is called Therapeutic Drug Monitoring (TDM).

- Algorithm of TDM :-



For Seizures - eg:- PHENYTOIN

Organ transplantation - eg :- CYCLOSPORINE

CVS disease - eg :- DIGOXIN

Psychiatric disorders - eg :- LITHIUM.

Seizures :- PHENYTOIN

Therapeutic range - 1 to 2 mcg/ml.

The phenytoin samples are collected only once for a dose as it has longer half life.

Organ transplantation :- eg:- CYCLOSPORINE.

The drug samples are collected generally for every 2-3 hours of administration.

If the dose is given for 1 week - every day.

for 1 month - every week samples are collected.

for 3 months - every month samples are collected.

This drug is given for organ transplantation patients as immunosuppressant to prevent graft rejection.

The TDM should be performed for this drug so as to prevent the disease from further progression. So TDM is necessary for this drug.

The samples are collected in trough phase or at pre-dose phase i.e, before administration of 2nd dose. (C_0) and also at the 2nd dose administration (C_2)

If samples are collected at pre dose phase, it is used to evaluate nephrotoxicity.

If samples are collected at 2nd dose administration i.e, C_2 then it is used to evaluate both nephrotoxicity and hepatotoxicity.

- The indications / levels / concentration of drug samples & observations.

Type of transplant	Type of sample (C_0) (mg/dl)	(C_2) (mg/L)	Observations.
Hepatic	200	400	1.4-2 — 15 days post transplant
	125	275	1.2-1.8 — 2-3 month post transplant (good renal function)
	100	125	1.2-1.8 — 2-3 months post transplant (bad ~~good~~ renal function)
	100	150	0.7-1 — ~~2-6~~ months post transplant
	75	150	0.7-1 — 1 year post transplant.
Renal	250	300	0.8-1.2 — 2-3 months post transplant
	100	200	0.6-1 — 6 months post transplant
Cardiac	250	300	- — initial
	100	200	0.3-0.4 — 2-3 months post tranplant

- The immunosuppressants dose must be reduced for every visit of the patient, so as to improve the immune response of the patient.

* CV (cardiovascular) diseases :- eg :- DIGOXIN
  Therapeutic range - 1 to 2 mcg/ml.
  1 mcg/ml = 1.3 n mol/ml

- Serum drug concentration is attained with in 5-7 days with 3-5 half lifes of drug.
- The sodium and potassium levels need to be monitored during the therapy.
- Samples are collected in the trough phase or pre-dose phase.
- The ~~toxicity~~ effects - nausea, vomiting, abdominal pain, confusion etc.

Psychiatric disorders :- eg :- LITHIUM.

- Therapeutic range - 0.4-0.8 mmol/ml
  Toxic range - >2 mmol/ml.

Serum drug concentration is attained for 12 hours and sample is collected after 12 hours of drug administration.

- If drug is given weekly - daily sample collected
  for 1 month - every week sample is collected.
  for 6 months - every month sample is collected
  for > 6 months - every 4-6 months sample is collected.

- Lithium drug causes the renal and hepatic failure due to the longer half life and drug accumulation / decreased renal clearance from the body.

effects (toxic) :- Polyurea, polydypsia, ECG changes, hypothyroidism, weakness, confusion etc.

30) @ Parameters taken into consideration for dose adjustment in renal failure patients:-

The two parameters that are considered for dose adjustment in renal failure patients are drug clearance and elimination half life of drug.

* Method I - for drug clearance:-

Equation - $$Ca_{av}^{\infty} = \frac{F D_0}{Cl_T \tau}$$ → for first initial dose

where F - bioavailability
D_0 - initial dose
τ - dosing interval
Ca_{av}^{∞} = average concentration of drug
Cl_T = Total clearance of drug
$\frac{D_0}{\tau}$ = Dosing rate.

- In normal patients; $$Ca_{av}^{\infty} = \frac{D_0^N}{Cl_T^N \tau^N}$$

where N = normal patients.

- In uremic patients; $$Ca_{av}^{\infty} = \frac{D_0^U}{Cl_T^U \tau^U}$$

where; U = uremic patients.

In renal impaired patients the glomerular filtration rate (GFR) is calculated with respect to uremia; so the average concentration of the drug should be changed to

dose in uremic patients.

$$\therefore \boxed{D_0^U = \frac{D_0^N \, Cl_T^M \, \tau^U}{Cl_T^N \, \tau^N}}$$

In uremic patients, the dose and clearance are variable but the dosing interval (τ) is constant.

$$\therefore \boxed{D_0^U = \frac{D_0^N \, Cl_T^U}{Cl_T^N \, \tau}}$$

D_0^U = dose in uremic patients

Cl_T^U = Total clearance in uremic patients

Cl_T^N = Total clearance in normal patients

D_0^N = dose in normal patients.

For infusion (IV) $\boxed{D_0^M = \frac{R_0}{Cl_T^N}}$

in uremic patients $\boxed{D_0^U = \frac{R_0}{Cl_T^U}}$

where R_0 is the infusion rate of given drug.

* Method II :- dose adjustment parameter base on elimination half life of drug :-

- In the uremic patients, there is increase in the rate of elimination half life of drug and decrease in rate of elimination of drug.

- Dose adjustment is done by decreasing the dose and maintaining frequency as constant or the frequency is changed or decreased with constant dose.
- If the nephrotoxicity is the ADR of drugs administered, then the dose must be calculated prior the administration into patients.
- In normal patients, the therapeutic monitoring is done by maintaining average concentration. When the clearance of drug in uremic patients is equal to distribution, then;

$$D_0^U = \frac{D_0^U k^U}{k^N}$$

$[\because Cl_T = K_E V_d$
V_d - constant$]$

- The above formula is used to calculate the direct estimation of dose in uremic patients. If the dose is undetermined, then indirect parameters are calculated.

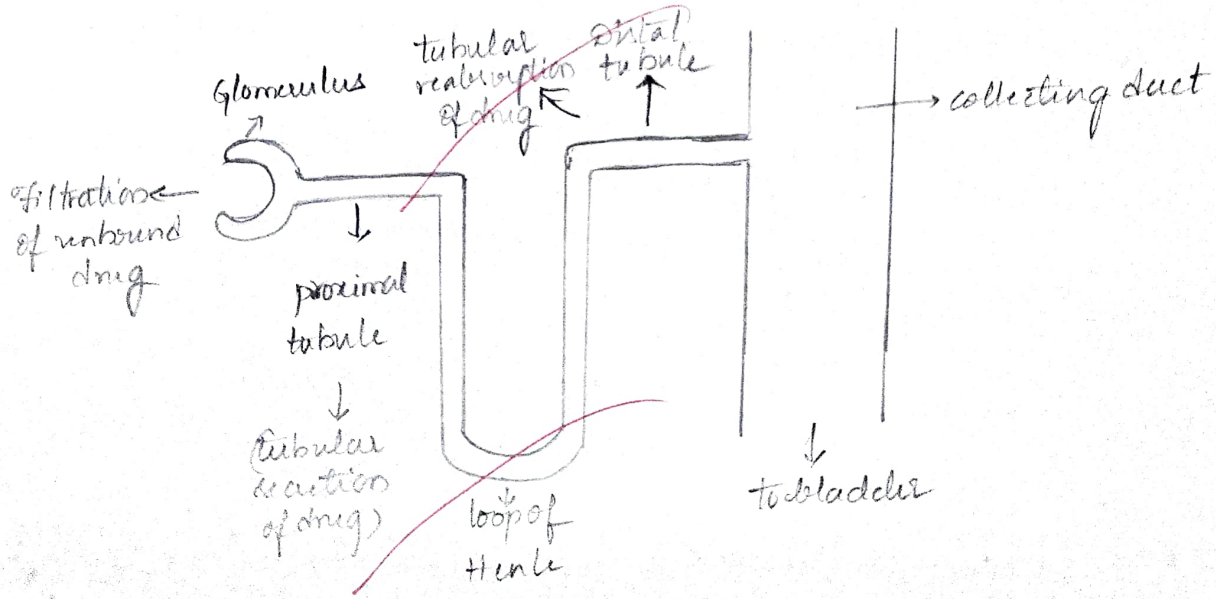
* Assumptions for calculation of indirect parameters:
  (i) If the renal elimination constant (k_R) is directly proportional to the renal clearance of the drug, then if elimination decreases, clearance also decreases.
  (ii) The non-renal clearance is constant.
  (iii) In case of renal failure, the renal clearance decreases and volume of distribution increases for a drug.

3. b&i) Measurement of GFR and Cdr :- measured in renal failure.

* Measurement of Glomerular filtration rate (GFR)

Some drugs are biomarkers for calculating or measuring the GFR value. The characteristics of drugs which can be biomarkers for GFR measurement are-

- The drug should truly filtered through glomerulus
- The drug should not be reabsorbed or secreted through tubules.
- The drug should not get metabolised.
- The drug should not be protein bound.
- The drug should not alter the hepatic clearance or impair the renal clearance.
- The drug should be non-toxic.



(Renal clearance of a drug)

- The drug infused should be of sufficient dose which reflects the simple and accurate quantification in serum(blood) and urine samples.

* Inulin fulfills the above characteristics of a ideal biomarker for measuring GFR.

+ It is infused and the steady state concentration is calculated
- It is a time consuming process and drug should be infused until stead state concentration.
- Inulin is a foreign product which has to be administered into the body. It is used to detect the renal damage extent.
- Creatinine: It is the end product of skeletal muscle metabolism and excuted as creatinine phosphate.
  - Creatinine is an endogeneous product & Inulin is a foreign product.
  - The creatinine is secreted into the renal tubules.
  - Creatinine is also used as the biomarker for the GFR measurement.

* Inulin is measured by $\frac{\text{IV infusion rate of Inulin}}{\text{Steady state concentration of Inulin}}$.

- Creatinine can be used to measure the renal damage in the body and it is most widely used.

- BUN (Blood Urea Nitrogen) lab evaluation is also used as biomarker
- The BUN contains urea - which is the end product of protein metabolism and its normal value ranges between 8-20 mg/dl.
- The BUN is reabsorbed and the tubular secretion is less than that of Inulin and creatinine, so it is not widely used as a biomarker.
- The Inulin is quantitative measurement of GFR which estimates its extent of renal damage.
- The creatinine and BUN are non quantitative measurements of GFR which doesn't determine extent of renal damage

* Measurement of Creatinine Clearance (Cl_{cr}) :-

- The serum concentration of creatinine is similar to the clearance (renal) of creatinine; so the serum concentration is constant for creatinine.
- If The serum concentration levels are increased that leads to decreased GFR rate and indicates renal damage.

→ Measurement of creatinine clearance (clcr) :-

$$Cl_{cr} = \frac{\text{rate of urine concentration of creatinine}}{\text{rate of serum concentration of creatinine}}$$

$$\boxed{Cl_{cr} = \frac{C_u V \times 100}{C_{cr} \times 1440}}$$

where, C_u = concentration of creatinine in urine
V = volume of urine

C_{cr} = concentration of creatinine in serum

Cl_{cr} = creatinine clearance.

Cock-croft gault equation:

- The creatinine clearance is measured by using Cockcroft gault equation.

$$Cl_{cr} = \frac{140 - \text{age (in years)} \times \text{weight (in kgs)}}{72 \times Sr_{cr}}$$

where Cl_{cr} = creatinine clearance

Sr_{cr} = Serum creatinine concentration)

*While calculating the creatinine clearance, the serum concentration should be constant and ideal body weight should be maintained.

- If less than ideal body weight, then the ideal body weight is included.

Ideal body weight :- For Males — 50 kg + 2.3 kg for every inch increase after 5 feet

For females :- 45.5 kg + 2.3 kg for every inch increase after 5 feet.

Creatinine clearance for children

0-1 year ⇒ $Cl_{cr} = \frac{0.48 \times \text{height (in cms)}}{Sr_{cr} \text{ (in mg/dl)}} \times \frac{\text{body surface area}}{1.73}$

where Sr_{cr} = Serum creatinine concentration

Cl_{cr} = creatinine clearance.

2-18 years $\Rightarrow Cl_{cr} = \frac{0.55 \times \text{height (in cms)}}{S_{Cr} \text{ (in mg/dl)}} \times \frac{\text{body surface area}}{1.73}$

40) (a) Causes of Renal impairments:- Various causes of renal damage are

- Hypertension
- Diabetes mellitus
- Drug toxicity eg:- Aminoglycosides, antibiotics etc
- Injury (Acute) to the kidney → kidney damage → Uremia
- Due to drug induced etc (Aminoglycosides, PHENACETIN)
- Hypovolemia condition.
- Drug accumulation and altered functioning.

Pharmacokinetic considerations :-

- The metabolism, excretion (clearance), bioavailability, volume of distribution, mesenteric blood flow will alter or decrease in condition of renal damage.
- The volume of distribution considers the plasma and tissue binding and total body water distribution.
- The volume of distribution depends on the plasma, tissue binding and total body water content.
- In the uremic patients, if weakly acidic drugs are given the renal clearance, volume of distribution decreases.
- If weakly basic drugs are given, the volume of distribution is unchanged or unknown.

- If the drugs bind to the plasmaproteins, the clearance decreases and toxicity increases.
- If the renal clearance is decreased, free drug concentration increases and leads to toxicity.
- Due to free drug concentration, the volume of distribution increases and leads to dominant effect and decreased renal clearance (toxicity in the body).
- The total body clearance is decreased due to the increased reabsorption (tubular) and decreased tubular secretion and hepatic clearance from the body.

4 b) **Protocol for Therapeutic Drug Monitoring:-**

-The protocol format for Therapeutic Drug Monitoring is as follows:-

1. Title of the study / project
2. Investigators - i. chief Investigator
   ii. Joint Investigator
   iii. Co-Investigator - (a) Clinical investigator
   (b) Research fellow.
3. Place of the study
4. Patient / subject selection place.
5. Need for the study (TDM study)
6. Objectives for the TDM study
7. Criteria for selection of subjects (patients)
8. Patients histories.

9, Withdrawl of blood samples and storage of blood samples.

10, Instrumentation for :-

a, measurement of drug levels in sample

b measurement of clinical parameters (like (ECG, EEG, respiration etc))

11, Report preparation

12, Clinical Interpretation.

30/30

Dh.

12/03/2020
Thursday.

Mid Examinations - III

20) Pharmacogenetics:-

The study of affect of genes and its alleles on drugs is known as pharmacogenetics.

Genetic polymorphism in drug metabolism:-

- Genetic polymorphism :- Existence of number of similar genes or alleles distributed in a set of population.
- Drug metabolism:- The metabolism of drug is conversion of xenobiotics or molecules into small molecules that are required for elimination from the body. The metabolism is processed to convert the drug into hydrophilic form for excretion.
- The metabolism of the drugs undergoes in 2 phases/reactions

  Phase-I - Oxidation, Reduction, Hydrolysis

  Phase-II - Methylation, acetylation, sulfation and conjugation.

These reactions are phases are required to convert the lipophilic insoluble drug into hydrophilic water soluble forms that can lead to excretion of drug from the body and preventing drug accumulation of toxicity.

- The metabolism is divided into 2 phases:-

  Phase I reactions :- also called as functionalization reactions.

Phase II reactions - also called as conjugation or synthetic reactions

- The metabolism mainly occurs in the liver as the target organ and the enzymes present in liver will metabolise the drugs.
- The organs also responsible for metabolism are - lungs, kidneys, skin etc.
- The genetic mutations or polymorphs can lead to changes in the activities of drug metabolism.
- Genetic polymorphism :- The metabolism changes from person to person due to inter individual variability.
  - The metabolism also changes in a subgroups of a population due to changes in the genes or alleles.

Polymorphism :- The changes in the genes or alleles that codes the proteins or enzymes responsible for metabolism is known as polymorphism. The mutations or changes can lead to defective alleles or nullified alleles that reduce or inhibit or induce the metabolism

Single nucleotide polymorphism :-

The mutation in single gene that code for one allele that is responsible for various metabolic processes is known as single nucleotide polymorphism and the alleles are single nucleotide polymorphs.

- There are different types of metabolisers in genetic polymorphism

1. Poor metabolisers :- These contain two defective alleles in the nucleotide and combination of those leads to no enzyme

Eg :- $CYP_2D_6 *4 / *5$; ~~$CYP_2D_6 *4 / *4$~~ .

(ii) Intermediate metabolisers:-

These contain one defective allele and one wild allele in the nucleotide sequence

(iii) Normal metabolisers:-

These contain ~~one~~ two wild alleles in the sequence. The presence of wild allele represents normal functioning of enzyme.

Eg:- $CYP_2D_6 *1/*3$

(iv) Extensive metabolisers:-

These contain one wild allele and one amplified allele or gene.

Eg:- $CYP_2D_6 *1/*2$

$CYP_2D_6 *A/*1A$

$CYP_2D_6 *1A/*5$

(v) Ultrarapid metabolisers:-

These contain two amplified genes or alleles in nucleotide sequence.

Eg:- $CYP_2D_6 *2/*3$

→ The enzymes that are less metabolised will result in increased substrate concentration and the enzymes that are highly metabolised leads to decreased substrate concentration.

* After the formation of polymorphs, they are divided into inducers and inhibitors.

The poor metabolisers and extensive metabolisers contain both inducers and inhibitors.

- Poor metabolising inducers :- This will lead to increase substrate concentration and decreased enzyme activity

This will lead to toxicity and drug interactions.

- Extensive metabolising inducers :- decreased substrate concentration increased elimination of drug.

- Poor metabolism inhibitors :- leads to toxic interactions & no toxicity

- Extensive metabolism inhibitors :- The effect of enzyme decreases leads to more concentration of drug and drug interactions, toxicity.

*Examples of Phase-I metabolisers :-

CYP_1A_1	CYP_2C_9	CYP_3A_4
CYP_1A_2	CYP_2C_{19}	CYP_3A_7
CYP_1B_1	CYP_2D_6	
CYP_2C_8	CYP_2E_1	

alcohol dehydrogenase, aldehyde dehydrogenase etc.

i) CYP_2C_9 :- This cytochrome enzyme is most commonly involved in metabolism of drugs.

Eg :- DEBRISOQUINE which is antihypertensive drug. When the genetically decreased content of CYP_2C_9 occurs the metabolism of this drug decreases. The mechanism is hydroxylation In whites, 5-10% of metabolic activity decreases

- This enzyme has 2 alleles - defective allele (decreased activity)
nullified allele (no activity)

ii) CYP_2C :- This subfamily is responsible for 18% of CYP450 enzymes involved in metabolism of drugs.

- CYP_2C_{19} :- Eg:- MEPHENYTOIN.

This drug will get metabolised by CYP_2C_{19} enzyme. There is decreased activity of enzyme when defective allelisare formed. There will be 18% decreased affect in asians, Caucasians etc.

- This enzyme also metabolises Diazepam, cyclosporine etc.

* CYP_3A_4 :- This enzyme is most commonly involved in metabolism of many drugs. Eg:- Digoxin.
This enzyme donot contains defective and nullified alleles.

* Examples of phase-II metabolisers:-

i) N-acetyl transferases - NAT_1, NAT_2
ii) Sulphonyl transferases
iii) Catechol-O-Methyl transferases
iv) UDP-glucuronosyl transferases - UGT_1, $UGTP_1$
v) $GSTM_1$, $GSTM_3$, GST_1, $GSTP_1$.

i) N-acetyl transferases :- NAT_1 have 2 alleles.

Eg:- ISONIAZID → fast acetylaters
slow acetylaters.

slow acetylators - 10% Japanese
20% chinese
60% Caucasians.

NAT_2 contains one allele and 17 subfamilies. The major and common allele is NAT_2 8,.

30) a) Genetic polymorphism in drug transport :-

- Drug Transport is the transfer of the drug from absorption site to the target (specific) site in the body.

* Advantages of drug transport - Target specific action.
Increased activity.
decreased interactions & accumulation

There are 2 types of drug transport mechanisms
- Active transport mechanism and passive transport mechanism.
- Active transport mechanism utilises the ATP - it is the site specific ligand binding mechanism.

→ The drug transport is mainly performed by influx and eflux proteins.
- Based on the transport of drugs and mechanism of transport the metabolism & excretion of drug depends.

- Influx transport

Polymorphs are transported through influx proteins

↓

Increased influx of nutrients and other ions into the cell

↓

Leads to growth of cancer cells

Eflux transport.

Polymorphs transported through eflux proteins

↓

eflux of drug and decrease in concentration of drug inside the cell/tissue

The drug transport mainly undergoes by 2 transporters.
ABC (ATP Binding Cassette) and Solute carriers.

ABC (ATP Binding Cassette)

There are subfamilies in the ABC transporters. The most active transporters are ABC - A, B, D, G.

The energy utilised by ABC is through ATP. These can develop multidrug resistance

This is the primary carrier

The mechanism is efflux of proteins

Eg:- of subfamilies

ABC - A
ABC - B
ABC - D
ABC - E
ABC - F
ABC - G

Solute Carriers

The solute carriers also contain the subfamilies.

The energy source is through electrochemical gradient.

This is the secondary carrier

This is bidirectional but influx is dominant.

Eg:- of subfamilies

SLC - 10
SLC - 22
SLC - O

Examples of drug transporters :-

- P-Glycoprotein (PGP) - it is the subfamily B and code 1

  Pgp B1

- Multidrug Resistance 1 - MDR-1 protein.

Site of Transport	Function
Liver - bile Kidneys - urine Placenta - barrier Brain - Blood.	Elimination Excretion ensures the protection of foetus ensures that the entry of drugs into the brain.

Mechanism of PGP transport/binding:-

Substrate Drug binds to PGlycoProtein

↓

The ATP binds to inner side of protein

↓

Hydrolysis of ATP to ADP and Pi

↓

Entry of substrate drug into the cell.

3(a.i) Genetic polymorphism in drug targets

- The target of the drug to is to ensure site specific action in the body.
- The genetic polymorphism in drug target can lead to changes in the action of drug or resistance to a drug.

* Advantages of drug target - Site specific action.
  - Prevents drug toxicity
  - Enhances therapeutic activity.

* Mechanisms of drug target - (i) Active drug targetting
  (ii) Passive drug targetting.

i) Active drug target:- The site specific ligand target is seen in active drug target mechanism.

The mechanisms involved are:-

a) Biochemical targetting :- the cells, cell organelles are targetted.

b) Physicochemical targetting :- based on magnetic resonance and ultrasound procedures.

* Mechanisms of Drug targetting:-

i) Active targetting :- Order 1 - targets on tissues
Order 2 - cells (tumour cells)
Order 3 - cell organelles (DNA, RNA etc)

ii) Passive targetting:- Includes 3 mechanisms.

a) Pro drug formation.
b) tumor micro environment
c) Deposition of drug.

a) Passive targetting involves the formation of prodrugs.

Eg:- i) Acetyl morphine which is a heroine derivative is converted into active drug Morphine.

ii) Prednisone is converted to active drug prednisolone

b) Tumor specific environment - ferro fluid is a fluid that is monitored by magnetic resonance. The ferrofluid is given along with drug which is used for target action on the tumor cell.

c) Transdermal route can enhance the target specific action.

→ Genetic polymorphisms affecting drug target:-

Eg:- VKORC1 (Vitamin k epoxide reductase enzyme)

VKORC1 is used to detect warfarin resistance.

Polymorph type	Dose of warfarin	Phenotype resistance
Warfarin drug	4 mg	Moderate resistance
A 41 S	4-16 mg	Moderate resistance
R 58 G	16-34 mg	major resistance
V 66 M	31 mg	major resistance
L 28 R	>45 mg	severe resistance
V 45 A	INR is not reached at any dose level	severe resistance

4A) a) Extracorporeal methods of removal of drugs:-

The removal of drugs outside the body is known as extracorporeal method of removal of drugs.

- These are used in conditions of End Stage Renal Disease and intoxication or poisoning conditions.
- The undesired levels of drugs in the body can also be removed by these procedures.

Types of Extracorporeal methods/techniques:- i) Dialysis
ii) Hemoperfusion
iii) Hemofiltration.

1) Dialysis :- Dialysis is performed to remove the drugs and wastes from the body. It is mostly performed in end stage renal disease & acutes conditions.

This is of 2 types - a) Hemodialysis
b) Peritoneal dialysis.

a) Hemodialysis :- The process of hemodialysis is diffusion mechanism.

- This is used to remove the metabolic wastes from the body.
- Heparin is required to avoid the clotting of blood outside the body.
- It is performed 2-3 times weekly as per the condition of the patient. The arteriovenous grafting is done for catheter placement.

b) Peritoneal dialysis :- The mechanism is diffusion.

- The peritoneum membrane is the barrier for the peritoneal dialysis.
- The dialysate in both hemo & peritoneal dialysis contains water, dextrose, electrolytes and other elements.
- The peritoneum surgery is done to place the catheter for dialysis.
- The surface of peritoneum is 1-2 m^2 and the molecular weight is <30,000 daltons.
- It is easy to perform and hospitalization is not required. The dialysate is 2 litres and it should be changed for every 4-6 hours.

(ii) Hemoperfusion:-

- It is used as an alternative method of hemodialysis and hemofiltration.
- The membrane used in hemoperfusion contains soluble cellulose filters.

(iii) Hemofeltration:-

- The hemofiltration is performed when only the blood cells need to be detoxified and filtered.
- The adsorbant material is used which is made up of activated charcoal and amberlite.

(iv) Continuous Renal Replacement therapy:-

- It is done for the end stage renal disease patients.
- It has 2 methods - Continuous veno-venous hemofiltration (CVVH) and Continuous artero-venous hemofiltration (CAVH)
- This method is used to clear the creatinine with a rate of 10ml/min.

→ Factors affecting the dialysis:-

(a) Absorption into plasma:- GLUTETHEMIDE is a sedative and hypnotic drug which is used as alternative to barbiturates

(b) Protein binding of drug:- protein binding of drug leads to infiltration & accumulation of drug eg:- PROPRANOLOL which have 94% protein binding capacity.

(c) Molecular weight of drug:- If the drug has >500 daltons of molecular weight, it doesn't get filtered.

Eg:- VANCOMYCIN - which has molwt of 1800daltons.

d Volume of distribution :- If the volume of distribution increases the flow rate of drug in dialysate decreases.

Eg:- DIGOXIN - has V_d of 200 - 300L.

- The rate of drug flow increases when the dialysate fluid rate increases.

Dialysance :- The rate at which the blood flows into the dialysis machine is known as dialysance.

$$Cl_D = \frac{Q(C_a - C_v)}{C_a}$$

where - Cl_D = Dialysance

Q = flow rate of blood.

C_a = concentration of drug in arterial flow

C_v = concentration of drug in venous flow.

The average clearance of drug is affected by the clearance (total) of the drug from the body. If the clearance of drug is 30% or more than 30% then clearance of drug decreases bioavailability

$$Cav = \frac{FD_0}{(Cl_T - Cl_D)\tau}$$

where Cav = average concentration of drug

F - bioavailability

$\frac{D_0}{\tau}$ - dosing rate.

The half life in dialysis patients is as follows

$$Cl_T = \frac{(0.693)\,Cl_T}{(t_{1/2})\,Cl_D} \quad \text{(normal)}$$

in dialysis patients - $$Cl_T = \frac{0.693}{(t_{1/2})(Cl_D - Cl_T)}$$

b(a:) Effect of hepatic disease in pharmacokinetics of the drug.

- The liver failure is a condition in which there is decrease in the activity (metabolism) of functioning of liver in the body.

Etiology:- Infections.
Comorbid conditions.
Hepatic damage

Types of liver failure:- Acute liver failure
Chronic liver failure

Parameters to be considered in liver failure patients for dose Calculation:-

- severity of liver failure.
- stage of liver failure.
- Symptoms of liver failure etc.

Diagnostic tests done for assessing liver failure:-

- SGOT - 6-40 IU/L
- SGPT - 7-56 IU/L
- ALP - 41-144 IU/L
- Serum Total Bilirubin - 0.6-1.1 mg/dl
- Direct Bilirubin - 0-0.4 mg/dl
- Indirect bilirubin - 0-0.6 mg/dl.
-

- Serum Total proteins - Albumin
  - Globulin

Albumin : Globulin (>1)

Effect of Hepatic failure in pharmacokinetics of drugs:-

- The hepatic failure can lead to decreased metabolism of drugs in the body.
- The hepatic failure can also lead to renal failure even the liver is not a primary cause.
- Hepatic clearance and Intrinsic factor:-
  - The hepatic clearance can increase or decrease based on the condition of the patient.
  - The hepatic clearance situation can lead to impaired metabolism that leads to increased bioavailability of drug and systemic toxicity of the drug.

Hepatic clearance $Cl_H = \frac{Cl_{int}}{Q + Cl_{int}}$

The intrinsic clearance = Extraction ratio ER.

- The severity of liver failure can be calculated by Childpugh classification.

Condition	1 (Absent)	2 (minimal)	3 (severe)
Ascites	2	2-3	>3
Bilirubin (mg/dl)	3.5	2.8-3.5	>2.8
Albumin (g/dl)	<2	3-6	>6
Prothrombin Time	1.8	1.8-3.2	>3.2
Encephalopathy	None	1-2	3-4

Condition	a	b	c
Albumin	< 2	2-4	>4
Bilirubin	3.5	2.8-3.5	>2.8
Ascites	None	minimal	poor
Neurological problems	None	minimal	moderate
Nutrition	excellent	Good	poor

The severity assessed based on the score and dose adjustment is done.

(a) 5-6 – the maintenance dose is reduced to 50% after initial dose

(b) 7-9 – the maintenance dose is reduced to 25% in normal dose after initial dose

(c) 10-15 – no dose is calculated, drug not administered.

Considerations for dose adjustment in hepatic failure:

- The drug which has 20% clearance through liver should be adjusted.
- The drugs that are volatile and gaseous in nature should be administered as they eliminate through lungs.
- The dose adjustment must be done based on the severity of liver failure
- The sources of variation and drug interactions should also be monitored. The systemic toxicity should be avoided.

Dose calculation in Hepatic failure:

Model for dose adjustment in liver failure/disease (adults – MELD)

Dose adjustment = 4.38 (Sr. Bilirubin) + 9.57 (INR) + 6.43 + 4.8 (Sr. creatinine)

PELD (Pediatric) = 6.47 (Sr. Bilirubin) + 18.57 (INR) + 6.86 (Sr. creatinine) + 6.76

and in case of age < 1 year – 4.36 is added/substracted.

Mid exam marks scored by students are entered in the Mother register

SUB. CLINICAL PHARMACOLOGY AND THERAPEUTIC DRUG MONITORING (T5103)

S.no	Reg No	Name of the Student	I Mid Theory	I Mid Practical	II Mid Theory	II Mid Practical	III Mid Theory	III Mid Practical	Theory Avg of best 2 mids	Practical Avg of best 2 mids
1.	157N1T0002	Bandi Athika Sri	AB		28		28		28	
2.	157N1T0003	Jawalapuram Sri Lakshmi Priyanka	29		29		29		29	
3.	157N1T0004	Nemmavala Lakshmi Chaithra	27		30		29		30	
4.	157N1T0005	Achari Kandukuri Sri Vasavi	26		26		AB		26	
5.	157N1T0006	Challagundla Sufanya	AB		27		28		28	
6.	157N1T0007	Belbuttonda Harshavardhini	29		30		AB		30	
7.	157N1T0008	Karneni Hema	28		29		30		30	
8.	157N1T0009	Kowati Madhuri	26		29		AB		28	
9.	157N1T0010	Madala Mounisha	26		29		29		29	
10.	157N1T0011	Parepalli Jhansi	29		30		30		30	
11.	157N1T0012	Appitonda Ramya Sravanthi	27		30		29		30	
12.	157N1T0013	Veerabandi Sri Naga Surya Athika	27		30		30		30	
13.	157N1T0014	Cottapu Bhargavi	27		28		AB		28	
14.	157N1T0015	Shaik Hafeez Munisa	28		29		29		29	
15.	157N1T0016	Shaik Jareena	26		28		28		28	

PRACTICAL

Sno	Reg No	Name of the Students	I Mid Theory	I Mid Practical	II Mid Theory	II Mid Practical	III Mid Theory	III Mid Practical	Theory Avg of best 2 mids	Practical
16.	157N17C017	Shaik Tanisha Bibi	29		29		30		30	
17.	157N17C018	Sri Rama Sahithya	26	NO	28	NO	27	NO	28	NO
18.	157N17C019	N.V.V.Phani Manika	27	PRACTICAL	28	PRACTICAL	29	PRACTICAL	29	PRACTICAL
19.	157N17C020	Tellakula Tudraja Sahaw	28		29		12		29	
20.	157N17C021	Tanvir Tejaswi Priyanka	27		28		21		28	
21.	157N17C022	Fli Lavanya	AB		28		25		27	
22.	157N17C023	Kanchana Lavanya Pekka	28		28		27		28	
23.	157N17C024	Mylipilli Sandhya	18		AB		25		22	
24.	157N17C025	Mannepalli Raja Kumari	AB		29		29		29	
25.	157N17C026	Mattapati Sivakishori	AB		28		28		28	
26.	157N17C027	Paladugu Vishnu Priya	26		AB		25		26	
27.	157N17C028	M.N.S. Gayathri	23		26		28		27	
28.	157N17C029	Chinthapalli Sai	21		25		AB		23	
29.	157N17C030	Shaik Sofiya	AB	AB	AB	AB	AB	AB	AB	AB
30.	154317C009	K. Jyothirmayee	26		28		AB		27	

Sno	Reg No	Name of the Student	I Mid Theory	I Mid Practical	II Mid Theory	II Mid Practical	III Mid Theory	III Mid Practical	Theory Avg of best 2 mids	Practical
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30.	187 N IT 0101	Pothuri Lakshmi Meghana	26	O	28	No	AB	O	27	O
				P		P		P		P
31.	187 N IT 0102	V. Mohana Muthitha	25	R	28	R	28	R	28	R
				A		A		A		A
32.	187 N IT 0103	Ananthaveni Sirisha	AB	AB	AB	AB	AB	AB	AB	AB
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				T		T		T		T
				I		I		I		I
				C		C		C		C
				A		A		A		A
				L		L		L		L

Entered by : Dhanush.B

Exam Section Incharge

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Mid exam marks uploaded to JNTUK University online portal

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Upload PharmD I,II,III,IV & V Lab Internal

View PharmD I,II,III,IV & V Lab Internal

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Note:- If The Subtype is null then check your subject code..

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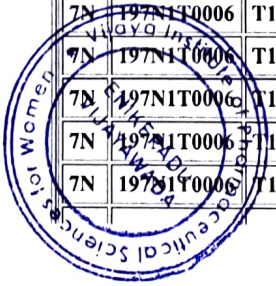

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