Pharmacology
&
Therapeutics
Laboratory Manual



1. Experimental Pharmacology: Rational Prescribing

Exercise on Prescription Writing

Introduction

Doctors in Bangladesh are licensed by the **Bangladesh Medical & Dental Council (BM&DC)** to diagnose & prescribe.

Bangladesh Medical & Dental Council (BM&DC)

- Is an independent body; constituted through an Act of Parliament; consisting of representatives from the profession, government and civil society, empowered to:
- register doctors to practice (within territorial jurisdiction of Bangladesh)
- take disciplinary action (including deregistration) for professional and ethical misconduct of registered doctors
- oversee the standard of medical education and
- set the minimum standards & criteria for selection of students & teachers, formulation of courses & curriculum and conduct of examinations, so that competencies of the graduates can be certified.

Most Medical Councils Recommend a 'Code of Good Medical Practice' to enable medical graduates to diagnose and prescribe. General Medical Council recommends as follows:

1. The importance of protecting life and health:

- 'an adequate assessment of the patient's condition ... (and) ... if necessary, an appropriate examination'
- 'providing or arranging investigations or treatments where necessary'

- 'competence when making diagnoses and writing prescriptions'

2. The importance of respect of autonomy:

- 'listen to patients and respect their views and beliefs'
- 'giving patients the information they ask for or need about their condition, its treatment and prognosis'
- 'respecting patients' privacy and dignity'

3. The importance of fairness and justice:

- '...(not allowing)... views about a patient's lifestyle, culture, beliefs, race, colour, gender, sexuality, disability age or social or economic status, to prejudice... treatments'
- '...(not refusing or delaying) treatment because you believe that patients' actions have contributed to their condition, or because you may be putting yourself at risk'

Almost every medical consultation result in a prescription.

Prescription

Is a written order by a registered doctor and is addressed to pharmacist to provide the patient the correct drug and the instructions on how to take it

The essential requirements of a prescription are that it should state

- what (drug & formulation) is to be given,
- to whom (patient) and
- by whom prescribed (doctor),

And give instructions on

- how much (dose) should be taken,
- by what route, how often (frequency) and for how long (duration) and
- also total quantity to be supplied

Prescribing guidelines

- Medicines should be prescribed only when they are necessary
- Benefit expected should be considered in relation to risk involved
- Treatment options with patient should be discussed (informed consent) so that patient is content to take the medicine
- Patient should be warned about side effects of drugs, how to avoid them, how to recognize them and when to report
- Prescription should be signed in ink and dated

Prescription format

- Name & Address of the doctor
- The date
- The patient's name address (must for Control drug) and age (legal requirement for children under 12)

Rx

- traditional esoteric symbol (said to be derived from the eye of Horus, ancient Egyptian sun god) – a sentimental link with past, meaning 'Recipe'-You take, which is addressed to pharmacist

sentimental link with past, meaning ‘Recipe - You take’, which is addressed to pharmacist

‘Eye of Horus’ sign, which may have been the origin of prescription symbol Rx

Falcon-headed Horus, son of Isis, the healing goddess and her borther and consort Osiris, was the guardian of health. The evil Seth (brother of Osiris & Isis), the god of diseases together with his sister and consort Nephthys destroyed the eye of Horus. TOTH, the source of all knowledge and physician to the gods healed the eye; sign of which is the origin of prescription symbol.

- **Name of the medicine, dose (per unit), route of administration, frequency of administration and duration of therapy**
    - **Name of the Medicine-**

      Prescribing by generic name (official, approved or International Non-Proprietary names INN) is recommended because of obvious advantages – uniformity (indicate pharmacological class), convenience (pharmacist may supply whatever proprietary formulations they have in stock) and economy; though prescribing by proprietary (brand) name is more common; because most physician want to ensure consistency of product in respect of quality and bioavailability and think that govt. control over quality of manufactured product is not as rigorous as it should be.

    - **Dose (per unit) of the medicine:**

      Unit dose strength should be in metric system, avoiding decimals, (500 mg & not 0.5g), if possible.

    - **Route of administration, frequency of administration and duration of therapy**

      should be clearly stated.

- **Direction to Pharmacist**
    - for preparing (if any) and dispensing (with labeling) of the medicine ordered. Label should contain name of the drug (or formulation) name of the patient and instructions for use with unit dose.
    - Total quantity to be dispensed should be written.

  Instructions for the patient

    - to be written in the ‘container’/phial by the pharmacist. These should be in the language understood by the patient and should be without any abbreviations.

Signature (initial) of the doctor

Prescription Writing

- **Prescription should be written legibly, dated, should state the name and address of the patient, and should be signed in ink by the prescriber.**
- **Mentioning the age of the patient is a legal requirement in cases of 'prescription only medicine' for children under 12 years.**
- **A prescription ordering control drug must in addition specify**
    - Prescriber's address.
    - patient's address
    - formulation and where appropriate the strength of the preparation.
    - total quantity of the preparation to be supplied or the number of does units in both words and figures.
    - Prescriptions ordering repeat on the same form is not permitted.

Here is the extracted text formatted for Microsoft Word. You can copy and paste this directly into Word:

Prescribing a Control Drug

- **The manufacture, import, supply, possession and prescription of narcotic and psychotropic substances (control drug) that are addictive on continued use are subject to control under Narcotic Control Act 1990.**
- **Such drugs however can be prescribed for use as medicinal products, subject to following requirement.**
    - No person other than a registered physician shall prescribe any of the control drugs.
    - Prescription for control drugs must be signed and dated by the prescriber and specify the prescriber's full address, and the prescription must always be written in the prescriber's own handwriting in ink.
    - The prescription must always state the name and address of the patient, the total quantity prescribed or the number of dose units in both words and figures, and the exact dose.
    - No person is allowed to purchase any control drug more than once under the same prescription.
    - It is recommended that a copy of the prescription for a control drug should be preserved by the prescriber for his/her own safety.
    - It is recommended that pharmacies maintain a separate register for dispensing of all A-Class and B-Class narcotics and psychotropic drugs, wherein the name and address of both the prescriber and the patient, and

name and quantity of the drug dispensed along with the date of dispensing are recorded.
    - A pharmacist is not allowed to dispense a controlled drug unless all the required information is given on the prescription.

Compliance

Patient Compliance

means that the patient actually follows the medical advice and instructions.

Patients' non-compliance is identified as a major factor in therapeutic failures.

Non-Compliance may Occur-

- The patient has not understood the instructions, so can not comply
- Poly Pharmacy
- Frequency & complexity of drug regimen
- Forgetfulness
- Lack of confidence on doctor and / or poor patient – doctor relationship.

Doctor Compliance

Doctor Compliance is about their obligations to fulfill their professional duties & responsibilities:

- Not to be ignorant
- To prescribe accurately
- To adopt new advances when they are proved safe and effective
- To tell patient what they need to know
- To warn about possible side-effects and measures to be taken to avoid them

Improving Compliance

Providing oral and written information adapted to patients' Understanding is essential for enhancing compliance

Patient should be told about

- An account of the disease and the reasons for prescribing
- The alternate therapy available and compared
- The name of the medicine
- The objective to treat / control disease / to relieve symptom
- When and how to take the medicine
- How long the medicine is likely to be needed
- How to avoid and / or recognized adverse effects and when to report

- Any interaction with food or other drugs

Preview of the Document Content (Sequential)

Expt. Ph-1 : Exercise on Prescription Writing

- Each batch of students will be provided with a set of prescriptions (see below for example) and will be asked to criticize them with regards to their format, legal and ethical aspects.
- Each student will be asked to write a model prescription based on the background information given above.
- Prepare a report in the book stating the objective of the exercise, making criticism of the prescriptions supplied with respect to format and writing a model prescription.

2: Essential Drug Concept: Exercise On Selection Of Essential Drugs for a community

Essential Drug Concept

- Essential Drug are those that satisfy the health care needs of majority of population.
- They should therefore be available at all time, in adequate amount, in appropriate dosage forms and in affordable price.
- WHO program on Essential Drugs has attracted much interest and approval in many countries including Bangladesh. WHO model list of Essential Drugs first published in 1977 has been updated several times including latest of 1999. This is intended to help countries to develop its own list.
- Bangladesh List of Essential Drugs, first published in 1982 and revised in 1996 contain 150 drugs (12 for use by village workers, 33 for use upto Thana Health Complex level and 105 for use upto Tertiary level). It has a Supplementary List of 100 drugs for use by Specialists. Bangladesh List of Essential Drugs is considered to be adequate to meet the common health needs of the majority of the population.
- Prescribing from Essential Drug List considered cost-effective, affordable and safe. Some however dislike the concept that some drugs are classed as essential while others by implication are deemed as non-essential.

Expt.: Exercise on selection of Essential Drugs for a Community

Objectives / Rationale:

- WHO has defined Essential Drugs as those drugs that satisfy the priority health care needs of the population.
- Prescribers should be encouraged to prescribe from within the 'Essential Drugs List'.
- WHO has laid down criteria to guide selection of Essential Drugs. They are -
    - Pattern of prevalent disease in a country (community) and the availability of health facilities & trained health man power.
    - List of drugs to treat those diseases along with adequate data on efficacy, safety, and cost.
    - Incase of two or more similar drugs, choice should be made on the basis of their relative efficacy, safety, suitability and cost.
    - Most essential drug(s) should be single. Combination can only be recommended, in case of proven advantage(s).
    - List should be periodically up-to-dated to account for changing disease pattern and availability of better drugs or formulation.

This exercise is aimed at selection essential drugs for 5 most prevalent disease in a community utilizing WHO criteria.

Methodology:

- Each group of students will select 10 diseases (5 communicable and 5 non communicable) diseases, prevalent in Bangladesh, on the basis of morbidity and mortality.
- That will be matched with the existing statistics provided by the Government of Bangladesh.
- 5 diseases out of these 10 will be selected by the group as the most prevalent diseases the community.
- Collect the Appropriate card for the Disease you have selected. This card (prepared by your teacher) list several drugs for use in the treatment of that disease mentioning their relative efficacy, safety, suitability and cost.
- Selected the essential drug(s) for each disease on the basis of the information (Efficacy, safety, suitability and cost), written on the card.

Write a report in the book starting:

- the objective the experiment you have just done methodology followed.
- provided the results in the tabular form (Tables are provided).
- Discuss the result.
- Make a comment on the Bangladesh List of Essential Drugs. Do you think that it would require urgent revision to make it upto date? cite at least one example to justify the revision.

Do you agree that prescribing from Essential Drugs List is considered cost-effective.

3. Experimental Pharmacology: Drug Information Sources

A comparative study of the 'prescribing information of drugs' as provided by the manufacturers product literatures and the the British National Fourmulary (BNF)

Objective & Rationale:

To ensure patient clinical needs, prescribing, should be appropriate. Appropriate prescribing is based on the choice of a drug for its effectiveness, safety convenience, and cost relative, to other drugs or treatment(s)

Increasingly doctors recognize that they need guidance to select the apporopriate drugs for their patients out of thousands of madicines so seductively promoted to them by the pharmaceutical industries.

Presently the only source of drug information that a doctor has easy access is the promotional literatues prepared by the drug manufactures whose principal aim seems to be Prescribe my drug. The question is- How much unbiased and reliable are these information for apporopriate prescribing?

The national formularies such a BNF (published by the British Medical Association and Royal pharmaceutical society of Great Britain biannually under the authourity of an independent Joint Formulary Commitee) provide sound up-to-date information on the selection, prescribing, dispensing, and administration of medicines. Basic information about drug is drawn through independent reviews of manufactures product literatures, medical and pharmaceutical, reports from requlatory and professional authorities and authentic national treatment guidelines.

The present study aims to compare the prescribing drug infornation provided by ten randomly selected Manufacturers Drug promotional Litratures with those of British Nation Formulary (BNF 47, March 2004) to see if manufactures promotional literatures can be recommended as authentic reference for appropriate prescribing.

Methodology:

Each group of student will be supplied with-

1. Ten randomly selected Manufactures product literatures as source of or prescribing information such asindication, caution, contraindications and side effects

2. BNF or BDNF (recent Ed) for corresponding information about the same drug

Result and observations

a) Compare the information provided by the Manufactures products literatures with those provided in BDNF.Record your observation in Table-1 (provided).

b) Provide the analysis of the result as per format in Table-2 (provided).

Write a report in your Experimental Note Book including the

a) Title of the Expriment

b) Objective& rationale of the Experment

c) Methodology

d) Result & observation

e) Discussion of the result along with example if any of the gross variations

f) Inference

g) Include the answer to the following Question in your report in the Experiment note book.

1. Name the drug compendia.

2. Authentic prescribing information can be obtained from National Formularies. Name some such fourmularies along with their publishers. How frequently they are updated?

3. How do official drugs having names included in pharmacopoeia (BP, USP, Euro.P, etc) differ with those that have only international non-proprietary name (INN)?

4.Prescribing drugs by generic(non-proprietary) name rather than by their proprietary names (trade name) is a more rational approach-Do you agree? Give reasons in support of your opinion.

5 What information about drugs do pharmacopoeias provide? Name some important pharmacopoeiasalong with the name of their publisher.

4: Drug Dosage Formulations

Exercise on Dosage Formulations

Drug Dosage Formulations Drug are usually prescribed as formulated preparations designated as medicine, only rarely are prescribed as pure chemical substance alone. Medicine is the formulated preparation of drug designed to achieve a predictable therapeutic response. It is the combination of **drug & excipients**.

Excipients are the pharmacology inactive additives included in the dosage formulation to provide varied and specialized pharmaceutical functions such as solubilization, suspension, emulsification, thickening, preservation, disintegration, etc.

Dosage should describe:

- The formulation of the drug
- Name of the drug
- Amount of the drug

Available dosage formulations are:

- A. Enteral Dosage Formulations
- B. Parenteral dosage formulations
- C. Topical dosage formulations

Enteral Dosage Formulations The term Enteron means gut. Enteral dosage formulations are administered through gastrointestinal tract.

These may be:

- Oral dosage formulations
- Buccal dosage formulations

- Sublingual dosage formulations
- Rectal dosage formulations

Oral Dosage Formulations & Oral Route Oral dosage formulations are usually intended for systemic effects resulting from absorption of drug from the gastrointestinal tract and less commonly for local action in the gastrointestinal tract.

Oral route is the most frequently used route for drug administration.

Available Oral dosage formulations are:

- **A.** Solid Formulations: Tablets, Capsules, Powder, Granules
- **B.** Liquid Formulations : Solution, Suspension, Emulsion

Solid Formulations

1. Tablet: Most frequently used solid Oral formulations obtained by compressing or moulding uniform volumes of particles (powder) that contains a single dose of active ingredient along with a number of excipients.

Used mainly for systemic action and occasionally for local effect at the site administration.

For systemic use tablets are designed to release the drug into the gastrointestinal system after disintegration and dissolution and thereafter to be absorbed into the circulation to reach the site of action.

For local use tablet are designed to release the drug in the mouth or the gastrointestinal tract.

Composition of a tablet:

a) Active ingredients

b) Excipients

Excipients : Pharmacologically inactive substance included in the formulations

- **a) Filler or diluent:** Normally a tablet should weight at least 50mg. So filler or diluent is added to increase the bulk volume of the powder if a low dose of drug is to be included per tablet. Examples of filler or diluent: Lactose, sucrose, glucose, etc.
- **b) Disintegrant:** Agent used in the tablets to ensure its disintegration into gut. Examples of disintegrants: Starch, cellulose, cross linked polyvinyl pyrrolidone etc.

- **c) Binder:** Also called adhesive and used to impart cohesiveness to the powdered material. It keeps the tablet intact after compression and imparts hardness or mechanical strength to the compressed tablet. Examples of binder: Gelatin, Starch, Sucrose etc.
- **d) Lubricant:** Agent used to prevent high friction of the tablet material with the die wall: Examples of Lubricant : Magnesium stearate, Stearic acid, Polyethylene glycol, Liquid paraffin, etc.
- **e) Glidant:** Agent used to improve flow ability of the powder during tablet production. Example: Silica, Magnesium stearate, Talc.
- **f) Antiadherent:** Agent used to prevent adhesion between the tablet powder and the punch faces and sticking to the punches. Example: Magnesium stearate, Talc, Starch.
- **g) Absorbent:** Substance used to absorb some quantities of fluid in an apparently dry state. Example: Microcrystalline cellulose, Silica
- **h) Other Excipients:**
    - Flavoring agent - For a more pleasant flavour or to mask an unpleasant one; e.g. orange flavor, banana flavor etc.
    - Coloring agent - Added to aid identification and patient compliance; e.g. caramel, brilliant blue, erythrosine, etc.
    - Sweetening agent - To avoid unpleasant taste and for better patient compliance; e.g. saccharine, mannitol, etc.

An antacid tablet contains

- **Active ingredients –** Al-hydroxide and Mg –trisilicate
- **Diluent &disintegrant-** Starch paste
- **Binder-** methyl cellulose
- **Lubricant-** Magnesium stearate
- **Flavoring agent-** orange flavor
- **Sweetening agent-** Na –saccharine

Types of Tablet: Depending upon the drug –releasing characteristics, tablet can be classified into two types-

- Immediate release tablet
- Modified release tablet:
    - Extended release tablet
    - Delayed release tablet

A. Immediate release tablet

This is the most common type that includes

- a. Disintegrating tablet.
- b. Chewable tablet.
- c. Effervescent tablet.

- d. Lozenges.
- e. Sublingual tablet &
- f. Buccal tablet

a. Disintegrating tablet:

Most common type; also known as plain or conventional tablet. It is designed to be swallowed and to release the drug in the gut in a relatively short time after disintegration. Then it is dissolved in the gastrointestinal fluid to be absorbed into the circulation.

Example: Tab. Paracetamol, Tab. Propranolol etc.

May be coated

- Sugar coated – to avoid unpleasant taste and for patient compliance (Example: Tab. Metronidazole, Tab. Multivitamin, etc.)
- Film Coated – to protect from light and moisture (Example: Tab. Ranitidine, Tab. Metronidazole)

b. Chewable tablet:

This type of tablet is chewed and thus is mechanically disintegrated in the mouth. It is then swallowed and dissolved in the stomach or intestine. Example: Tab. Antacid, Tab. Albendazole, Tab. Vitamin C. etc.

c. Effervescent tablet:

Dropped in a glass of water to liberate carbon dioxide before administration. This facilitates tablet disintegration and dissolution. Example: Tab. Acetylsalicylic acid, Vitamin tablet, etc.

These tablets should be packaged in such a way that they are protected against moisture – e.g. in a water-proof containers, in blister packs or Aluminium foils.

d. Lozenges:

Tablets that dissolve slowly in the mouth and thus release the drug to be dissolved in the saliva. Used as local medication in the mouth or the throat, e.g. local anaesthetic, antibiotic and antiseptic drugs or for soothing effect. Example: Tab. Strepsils.

e. Sublingual tablet & Buccal tablet:

Used for drug release in the mouth followed by systemic uptake of drug. A rapid systemic effect thus can be obtained avoiding first pass metabolism. Sublingual tablet

are placed under the tongue and buccal tablet are placed in the side of the cheek. Example: Tab. Nitroglycerine, Tab. Nifedipine.

B. Modified release tablet

a) Extended release tablet

These are designed to be swallowed and thereafter to release the drug slowly in the gastrointestinal tract; also known as slow release tablet, prolonged release tablet, sustained release tablet or controlled release tablet. An extended release tablet contains one dose of the drug to be released slowly for a period of about 12-24 hours at a nearly constant rate.

Can be categorized as

- Single unit dosage form – drug dose is incorporated into a single-release unit
- Multiple unit dosage form – drug dose is divided into a large number of small release units

Aim of these formulations is

- To increase the duration when a therapeutic drug concentration level in blood is maintained (Example: modified release formulation of Tab. Diclofenac sodium, Tab. Mebhydrolin, Tab Theophylline)
- To increase the release time for drugs that can cause local irritation in the gut (Example: modified release formulation of tab. Aspirin, Tab. Ferrous fumerate, etc.)

Prolongation of duration of action of drug reduces the frequency of its administration. The controlled release function of these tablets is accomplished by film coating, or by multiparticulate system. These tablets are made up of concentric layers of active drugs, each having separate coating with polymers like ethylcellulose and modified acrylate derivatives. After coating the particles are compressed directly into tablet. Different coatings dissolve at different times so that each layer of drug is released at different times.

b) Delayed release tablet:

These tablets are designed to release the drug from the tablet some time after administration. After the period has elapsed, the release is rapid. The most common example is the enteric coated tablet.

Enteric coated tablet:

May be coated with polymer insoluble in gastric fluid but readily soluble in intestinal environment. So disintegration is delayed until it reaches the intestine.

Tablet are coated

- To prevent gastric acid destruction of active constituents unstable at low pH
- To protect the stomach from the irritant effect of certain drug
- To facilitate absorption of a drug that is preferentially absorbed distal to stomach

Enteric coating is possible using both sugar –and film –coating techniques.

Example- Tab aspirin (enteric coated), Tab. ferrous sulfate (enteric coated), etc.

Delayed release tablet can also be combined with a slow drug release, e.g. for local treatment in the lower part of the intestine or the colon- Modified release formulation of mesalazine in the treatment of ulcerative colitis.

CAPSULES:

A pharmaceutical preparation made from gelatin or other suitable material which is filled with medicine to produce a unit dosage mainly for oral administration.

Types:

1. Hard capsule/ two – piece capsule
2. Soft capsule/ one-piece capsule

Both types of capsules contain gelatin, water, and other materials like preservative and process aids. Gelatin is prepared from collagen, the main protein of connective tissue. It is nontoxic, widely, acceptable, and readily soluble in biological fluid. When a capsule come into contact with GIT fluid the gelatin shell starts to dissolve. First the shell is invaded by aqueous solution, the capsule rapidly swells & bursts and release its contents into the gut.

Hard capsule

Consists of two pieces in the form of cylinders closed at one end; the shorter piece, called the cap, fits over the open end of the longer piece, called the body ; may be filled with different types of filling material - dry solid, Semisolid or liquid. Dry solid may be powders, pellets, granules or tablets.

Example: Cap. Ampicillin, Cap. Tetracycline etc.

Soft capsule

Also known as softgel a one –piece capsule having outer gelatin shell and liquid or semisolid fill matrix – the formulation of drug in the form of solution or suspension. The capsule consists of gelatin, water and a plasticizer. It may be opaque or transparent and can be coloured and flavoured if desired. It may be oval or oblong in shape.

Example: Cap. Vitamin A, Vitamin E, Cod liver oil capsule, etc.

Capsules may be

Swallowable, chewable, suckable, Twist- off, meltable

Composition of capsule:

A. Active ingredient/s B. Excipients

Excipients:

- **a) Diluent-** Lactose, etc.
- **b) Lubricants-** used to reduce powder flow, e.g.
- **c) Glidants –** which improve powder flow, e.g. silica.
- **d) Wetting agent-** which improves water penetration.
- **e) Disintegrants-** which produce disruption
- **f) Stabilizers-** To improve product stability.
- **g) Preservatives-** To prevent growth of fungi on the surface. Particularly soft capsules have preservatives. e.g. Sorbic acid, etc

Linctus:

A viscous preparation normally consists of a simple solution of the active agent in a high concentration of sucrose, often with other sweetening, agents or sorbitol and/ or synthetic sweeteners for diabetics. Usually used for relief of cough.

Suspension:

Suspension is a heterogeneous liquid formulation in which finely divided insoluble particles, generally greater than 1 um in diameter, are dispersed in a liquid or semisolid medium, usually aqueous. The insoluble solid particles constitute the disperse phase or the internal phase and the liquid or semisolid vehicle constitute the continuous phase or the dispersion medium.

Insoluble solid particles are kept suspended in the continuous phase by a suspending agent that reduces the interfacial tension between two phases. The suspended material tends to settle to the bottom of the container on standing that readily disperses into a uniform mixture when the container is shaken.

Example: Susp. Contrimoxazole, Susp. Antacid

Emulsion:

An emulsion is a system consisting of two immiscible liquid phases, one of which is dispersed throughout the other in the form of fine droplets. A third component, the

emulsifying agent is necessary to stabilize the emulsion. It reduces interfacial tension between two phases to make them miscible with each other. The phases that is present as fine droplet is called the disperse phase and the phase in which the droplets are suspended is the continuous phase. Most emulsion will have droplets with diameters of 0.1- 100 um and are inherently unstable system. An emulsion contains flavouring and colouring agent, preservatives, etc. Emulsions are two types • Oil in water (o/w) • Water in oil (w/o)

Examples of (o/w) emulsion: Cod liver oil, Castor oil, etc.

Dry Syrup:

Some drugs are physically or chemically unstable in aqueous solution or suspension. These drugs are supplied in the form of powder or granules in a suitable container. A given quantity of water is added in the container to reconstitute the solution or suspension just before use. The reconstituted solution or suspension has a shelf life of only a few (5-7) days.

Example: Susp. Amoxycillin, Susp. Cloxacillin.

Comparison of different liquid formulation with one another

Parameter	**mixture**	**Syrup**	**Elixir**	**Suspension**	**Emulsion**
Active Ingredient	Soluble	Soluble	Soluble	Insoluble in water	Immiscible liquid
Vehicle	Water	Water	Hydro-alcohol	Water	water/ oil
Special Excipients	-	Sugar	Sugar	Suspending agent	Emulsifying Agent
Other Ingredients	Colouring, flavouring, preserving	Colouring, flavouring, preserving	Colouring, flavouring, preserving	Colouring, flavouring, preserving	Colouring, flavouring, preserving

Parameter	mixture	Syrup	Elixir	Suspension	Emulsion
Use	Oral/ parenteral	Oral	Oral	Oral / topical/ Parenteral	Oral / topical/ Parenteral

Suppository:

Suppositories are solid conical formulations of drugs to be administered through rectal route (commonly, less commonly by vaginal & rarely by other routes). These soften and melt at body temperature and then drug is released and absorbed into circulation to exert systemic effect.

Example- For systemic effect: Paracetamol suppository, Diclofenac suppository

For local effect: Drug for treatment of haemorrhoid, Glycerin suppository.

Parenteral Dosage Formulation of Dosage

The term Para means beyond and Enteron means gut. So the word parenteral means beyond the gut. Parenteral Dosage formulations are the formulations that are administered by injection directly into the tissue fluid or blood bypassing the gut and limitation associated with oral administration.

Advantages of parenteral administration of drug include

- Faster & quicker action
- Suitable for emergency
- Gut and liver bypassed
- Can be given to unconscious, non- cooperative and vomiting patients

Disadvantages of parenteral administration of drug include

- Invasive technique, painful and requiring sterilization, aseptic means & skilled hand.
- Increased chance of hypersensitivity reaction and local tissue injury

Parenteral Dosage Formulation:

Injection are sterile solution/ suspension/ emulsion packaged such as it is suitable for administration by injection or sterile drug preparation that is to be administered by injection after addition of a suitable solvent/ suspending agent / emulsifying agent.

Preparation:

1. Preformed injection dispensed as solution/ suspension/ emulsion in ampoules or vials e.g. Inj. Gentamicin, Inj. Diazepam, Inj. Dexamethasone, etc.
2. Dry powder dispensed in vials to be reconstituted to solution/ suspension by sterile aqueous vehicle dispensed in ampoules, prior to injection (Example- Inj. Ampicillin, Inj. Amoxycillin, etc.)
3. Sterile intravenous fluid dispensed in plastic container – bottle or bag

Routes for injection:

- Intravenous injection
- Intramuscular injection
- Subcutaneous injection
- Intra- spinal injection
- Other less commonly used injections: Intra- articular, Intra- dermal, Intra- peritoneal, Intra- pleural, Intra- cardiac, Intra- arterial injections.

Intravenous injection:

Sterile water soluble preparation – directly to be injected into the systemic veins.

Can be given by two methods:

- **a. Bolus injection:** Certain volume of drug is forced directly into the vein by a syringe. Small volume of drug is injected by this route, about up to 50ml of drug can be injected at a time.
- **b. Infusion:** Drug is introduced slowly into the venous system by means of gravity through a channel. Large volume of drug formulation/ fluid (up to 2500ml/ day) can be administered by this method.

Intramuscular injection:

These formulation are introduced by a syringe directly into the mass of large skeletal muscle (deltoid/ biceps/ gluteus muscle/ rectus femoris etc. Small volume of drug (1-5 ml) can be injected by this route. These muscles are more vascular – so absorption is faster, less richly supplied by nerves – so mild irritants can be injected. Deep penetration is needed. Depot preparation can be given.

Example: Inj. Penicillin, Inj. Streptomycin, etc.

Subcutaneous Injection:

The drug formulations are injected into the loose subcutaneous tissue, absorption occurs slowly. This tissue is less vascular but is richly supplied by nerves, so that irritant drugs can not be injected.

- Self-injection is possible because deep penetration is not needed
- Should be avoided in shocked patients, where absorption could be greatly reduced because of vasoconstriction
- Repeated injection at a particular can cause lipodystrophy

  Example: Insulin injection.

Intra-spinal Injection/ Intrtheacal Injection:

This method involves introduction of drug directly into the subarachnoid space usually by lumbar puncture.

Advantages:Drug is injected directly into CNS

Disadvantages:Highly skilled personnel are required & strict aseptic precaution is essential.

Example: Spinal anesthesia, antibiotics for treatment of meningitis, encephalitis.

Methods for Delaying Absorption from Injection Site

Subcutaneous or intramuscular injection of drugs usually produces a faster action than oral administration; But the rate of absorption depends greatly on the site of injection and on local blood flow.

Absorption from the site of injection is increased by increased blood flow (massage following injection). Hyaluronidase (an enzyme that breaks down intercellular matrix) also increases drug absorption from the site of injection.

Sometimes it is desirable to delay the absorption from site of injection

a) To reduce systemic effect/ prolong local effect

Example: addition of adrenaline or noradrenaline (1:1000 to 1:80,000) to a local anaesthetic

(e.g. Xylocaine)

b) To prolong Systemic effect

Example:

1. Using a relatively insoluble 'slow release' formulation, for example, a poorly soluble salt/ ester/ complex injected either as an aqueous suspension or an oily solution:

- **Procaine penicillin:** injected as aqueous suspension & exerts a prolonged action Benzylepenicillin+procaine
- **Esterification of**

  i) Steroid- Medroxyprogesterone acetate

  Testosterone propionate

  ii) Anticychotics: Fluphenazine decanvate

2. Decreases their solubility in oil and slows their rate of absorption, when injected in any oily solution.
3. Changing the physical characteristics of a formulation

   Example: Insulin-Zn suspension

   Insulin forms a complex with Zn the physical form (amorphous/ Crystalline) of which can be altered by varying pH to influence the rate of absorption.

   - Fine amorphous suspension from which insulin is absorbed rapidly (soluble insulin)
   - Suspension of crystals from which insulin absorption is slow (Long acting insulin)
   - These can ve mixed to produce an intermediate but sustained effect (isophane insolin)
4. Subcutaneous Implantation of solid pellets

   Rate of absorption is proportional to the surface area of the implant

   Example: levonorgestrel, Hormonal contraceptives (norplant)

Topical Dosage Formulation and Topical Administration of Drugs

Topical Administration: Application of drugs locally on the screen and mucus membrane.

Topical medications usually consist of active ingredient incorporated into a vehicle that facilitates dispersion and absorption of drug from the site of application.

Purpose:

- Local effect
- Systemic effect

For local effect: on the skin, eye, ear, nose, oral, cavity, rectum, vagina, etc.

For systemic effect: Special delivery systems to deliver the drug through a rate limiting membrane at a certain rate into the subcutaneous tissue or on the mucus membrane from where it absorbed into blood to exert systemic effect.

Sites of Application: Skin, Eye, Ear, Mucus membrane of nose, oral cavity anal canal, vagina, GIT\

Formulations: Liquids, Cream, Ointment, Gel, Powder, Paste, Aerosols, Pessaries

Transdermal Delivery System (TDS)

A. Liquids may be solution / suspension/ emulsion containing one or more ingredients in a suitable vehicle.

Examples of solutions:

- Eye drops — Homatropin eye drop, Cloramphenicol eye drop, Ciprofloxacin eye drop, etc
- Ear drop — Cloramphenicol ear drop, Steroid ear drop, Antazol ear drop, etc.
- For Application on skin — Gentian violet lotion

Lotions are aqueous solutions or suspensions or emulsions containing active drug on a vehicle to be applied externally on the skin from which water evaporates to leave a thin uniform coating of powder.

Evaporation cools and soothes the skin, making lotions valuable to treat acutely inflamed areas.

If added, alcohol enhances the cooling effect and glycerol sticks the powder to the skin.

Example:

- Solutions: Lotio normal saline, Lotio KMnO4, Lotio 5% detol
- Suspensions: Lotio calamine
- Emulsions: Lotio Benzyl benzoate

B. Creams are semisolid emulsions for external application. These may be

1. Aqueous: oil-in-water (o/w), 2. Oily: water-in oil (w/o)

Aqueous cream: oil-in-water emulsions (vanishing cream), rub into the skin, the continuous phase evaporates and increases the concentration of a water-soluble drug in the adhering film to percutaneous absorption of drug.

Oily cream: water-in oil (w/o) emulsions, less greasy than ointment, spreadsmore readily and the evaporating water soothes the inflamed tissues. Examples: Betamethsone cream, Clotrimazole cream, etc.

C. Ointments greasy, semisolid preparation containing dissolved or dispersed medication usually in an anhydrous or fatty base. These are for external application on the skin or in the eye, ear or other mucus membrane. Examples: Betamethasone ointment, Neomycin + Betamethasone ointment, etc.

D. Gels are semisolid that release the contained drug through pores by diffusion. Examples: Diclofenac gel

E. Dusting powder: Finely divided (impalpable) insoluble powder for application to skin folds that dry, protect and lubricate those areas. Examples: Talc, Zinc oxide, etc

F. Paste: Ointment containing as much as 50% powder dispersed in a fatty base. Paste localizes the action of an irritant or staining material. Pastes lay down a thick unbroken, relatively impermeable film that can be opaque and act as an efficient sun filter. Players/ Skiers use it.

G. Aerosol: may function as drug delivery system for solutions, suspensions, powders, semisolids and emulsions topically for local action or systemic effect. Example: Nasal spray, Analgesic spray, Nitroglycerine spray

H. Pessary: Solid medicated preparation to be introduced into vagina where they release drug for local action.

Exercise on Dosage Formulations

You will be given demonstration in the class of several dosage formulations intended to be used orally, parenterally, topically or by inhalation.

For each of the formulation, demonstrated, observe & note the following information and write a report in the next few pages.

1. **Name of the Dosage formulation**
    - Non-proprietary (Generic Name)
    - Proprietary (Trade) Name
    - Name of the manufacturer
    - Whether BP/USP/INN has been quoted after Generic name? What do they signify?
2. **Types of formulation:** (If oral-solid or liquid, if liquid, suspension/elixir etc)
3. **Name of the active drug(s)**
4. **Possible excipents used**
5. **Prescribing information about the dosage formulation.** (Name, dose, indications, side-effects, cautions, contraindications etc)

5. Prescription Audit Exercise on Rational Prescribing & Use of Medicine

Introduction

The rational use of Medicines requires that patients receive medications:

- appropriate to their clinical needs
- in dose that meet their own individual requirements
- for an adequate period of time, and
- at the lowest cost to them & their community.

(WHO 1985)

Rational use of medicine includes the following criteria:

- Correct medicine;
- Appropriate indication
- Appropriate medicine, considering efficacy, safety, suitability, and cost;
- Appropriate dosages, administration, and duration of treatment;
- Appropriate patient-that is, no contraindication exist;
- Correct dispensing, including appropriate information for patients
- Patient adherence to treatment

5 Ds to remember easily

- **Diagnosis:** Based on sound medical knowledge
- **Drug (Medicine):** Appropriate medicine considering efficacy, safety, suitability and cost
- **Dosage:** Appropriate does and frequency in correct dosage form
- **Duration:** Appropriate duration of treatment
- **Dispensing:** Appropriate manner of dispensing containing understandable labeling

Prescription Audit Exercise of Rational Prescribing & Use of Medicine

Objectives:

At the end of the exercise, the students shall able to-

1. analyse the prescribing situations in order to assess the types and magnitudes of irrational prescribing and uses of medicines in the country
2. identify influences affecting prescribing behavior & measures to resist pressures for irrational prescribing
3. evaluate ethical, legal and economic issues in prescribing
4. understand the principles of rational prescribing.

Materials & Methods:

Samples of prescriptions have been collected randomly from patients of private practitioner of Dhaka City. No attempt has been made to group the prescriptions according to patient's sex, age or disease profile.

5 prescriptions are given to a group of 3-4 students to audit (analyse) them using the INRUD prescribing indicators. They are given 40 minutes to complete the analyses.

TABLE-I: INRUD PRESCRIBING INDICATORS

Prescribing IndicatorsNumber of prescriptions (n=)	**Results**
❖ Average number of drugs per prescription	
❖ Percentage of drugs prescribed by generic name	
❖ Percentage of prescriptions with antibiotics prescribed	
❖ Percentage of prescriptions with an injection prescribed	
❖ Percentage of drugs prescribed from Essential Drug List	

Prescribing IndicatorsNumber of prescriptions (n=)	Results
Whether prescription is complete with respect to a) format b) dosage & duration and c) patient medication information (PMI)	

All the groups in the class will reassemble after 40 minutes and will compile the individual group results into a combined one and present them in the following format.

Table-II: Results of Prescriptions (n=) Audit

Indicators	Results
Average drug per prescription	
Prescribed in generic name (%)	
Antibiotics prescribed (%)	
Injections prescribed (%)	
Prescribed from EDL (%)	

Indicators	Results
Prescription is complete with respect to a) format b) dosage & duration and c) patient medication information (PMI).	

The results will be discussed in relation to principles of rational prescribing.

6.Exercise on Selection of P-drug

Introduction

Good prescribing habit should begin before graduation. Students are encouraged to make rational prescribing choices and develop skill required to critically evaluate the drugs prescribed. Exercise on selection of P-drug provides the student a method for selecting appropriate treatment and an opportunity to develop problem solving skill. Students are therefore taught to develop standard pharmacological approach to common clinical conditions, selecting appropriate first choice drugs (P-drugs). These are not patient specific but appropriate to diagnosis.

Objectives

To develop a rational pharmacological approach for the selection of appropriate first choice drugs (P-drugs) for common clinical conditions.

Selection of a P-drug (often referred to as 'personal' drug) involves following steps:

i. Defining the diagnosis

ii. Specifying therapeutic objective(s)

iii. Making an inventory of effective groups of drugs

iv. Choosing an effective group according to criteria

v. Choosing a P-drug

- **Defining the diagnosis:**

  The patient problems are defined & a diagnosis is made

- **Specifying the therapeutic objective(s):**

  The therapeutic Objective(s) are specified i.e. what we want to achieve with the treatment

- **Making an inventory of effective groups of drugs for that objective:**

  Listing of at least 2-4 appropriate drug groups consulting objective drug information sources – such as National Formularies, Treatment Guidelines, Drug Information Bulletins, Textbooks and Journals, etc.

- **Choosing an effective group according to criteria:**

  of the 2-4, one most appropriate group is chosen comparing efficacy, safety, suitability and cost, and applying a scoring or ranking system

  - Efficacy – is compared on the basis pharmacodynamic considerations
  - Safety – is compared on the basis side effect profile
  - Suitability – applies to kinetic considerations matched with patient's factor (age, pregnancy, liver & kidney function etc.)
  - Cost – affordable prescribing

- **Choosing a P-drug:**

  A specific drug within the group is chosen. Same criteria of efficacy, safety, suitability and cost can again be used

Example:

Patient I: A 60-yr old man with no previous medical history, has had occasional attacks of suffocating chest pain during the last month, which began during physical labour and disappeared with rest. He has not smoked for 4 years. His father and a brother died of a heart attack. Excepting occasional aspirin, he has not used any medication. Physical examination reveals no abnormality blood pressure is 130/85, pulse 78 regular and body weight is normal. Clinical diagnosis is angina pectoris.

Selection of a P-drug for angina pectoris

- **Define the diagnosis**
  - Stable angina pectoris
- **Specify therapeutic aim**
  - Prevention of anginal symptoms
- **Make inventory of effective groups (describing dynamics, kinetics and possible adverse reactions)**
  - Nitrates
  - β-blockers
  - Calcium channel blockers
  - Potassium channel openers
- **Choose a group according to criteria (Using simple discription or a rating scale)**

Drug Groups	**Efficacy**	**Safety**	**Suitability**	**Cost**
Nitrates (tablet)				
β-blockers				
Calcium channel blockers (tablet)				
Potassium channel openers (tablet)				

- **Choose a P-drug according to criteria (Using simple description or a rating scale)**

Individual Drugs	**Efficacy**	**Safety**	**Suitability**	**Cost**
Bisoprolol (tablet)				

Individual Drugs	Efficacy	Safety	Suitability	Cost
Metoprolol (tablet)				
Atenolol (tablet)				
Propanolol (tablet)				

OR

Individual Drugs	Efficacy	Safety	Suitability	Cost
Glyceryl Trinitrate SR (tablet)				
Isosorbide dinitrate (tablet)				
Isosorbide Mononitrate (tablet)				