Formulation of drugs

1. Antibiotics
2. Antipyretics
3. Steroids
4. Injectibles
5. VitamineS

Dose oral :- 12.5 mg/kg - 250mg

1. ANTIBIOTIC

Example: Amoxycillin , Chloramphenicol

- It has a similar spectrum of activity to ampicillin but also inactivated by penicillinase. However it is better absorbed after oral administration than ampicillin.
- Amoxycillin is used for the treatment of some infections including otitis media and respiratory tract and urinary tract infections.
- **Availability tablets;** 250mg ,500mg **kid tablets ;** 125mg ,250mg **capsule;** 250 mg , 500 mg **Dry syrup ;** 125 and 250 mg per 5ml **Injection ;** 1ml ampoule (100mg/ml) , 250mg/vial **Drop** 10ml(100mg/ml)
- **Dose oral : Adult** 250mg every 8hour double in severe infection , 1g every 8h.
- **Precautions** :History of allergy; renal impairment; erythematous rashes common in glandular fever, chronic lymphatic leukaemia and possibly HIV infection (kidney failure)
- **Adverse effect** ;Nausea , vomiting ,diarrhoea ,rashes , hypersensitivity reactions

Material and methods

Material

Chloramphenicol (BioBasic©), hydroxypropyl methylcellulose (HPMC)tween 80 ,propylene glycol ,methyl paraben , soyabean casein digest, glucerin, Sodium hydroxide, Potassium hydroxide,Cellophane membranes,*E.coli*, nutrient agar

• Methods

- The experimental laboratory was conducted in stages.

Preformulation: Examination of the active substances used (chloramphenicol) by the monograph of the Indonesian Pharmacopoeia were:

Melting point determination of active substance

- Determined by the temperature at the time of chloramphenicol start to melt until becoming a liquid form. The result was compared with chloramphenicol monograph in the Indonesian Pharmacopoeia.14

Standard curve of chloramphenicol

- Chloramphenicol weighed 500 mg and dissolved in 100 ml of phosphate buffer pH 7.4 to obtain a stock solution of 5000 ppm. From a stock solution did variety dilutions 6, 8, 10, 12, 14 ppm. The absorbance was measured at a wavelength of 280 nm with a spectrophotometer UV/Vis. Absorbance obtained, was used to form a standard curve chloramphenicol.

Potential testing of chloramphenicol

- Sample solution and standard solutions, that has been diluted were filled into each reservoir about 50µl using a micropipette. The Petri dishes were incubated at 37°C for 18-24 h. Measured and recorded diameter clear zone (zone lysis). Calculated the potential of chloramphenicol.

Hydrogel formulations

- Different formulations were prepared . The drug solution was added to the hydrogel base while stirred. So that no foam was observed. The buffer solution was added to the formulation, and the following by addition of distilled water up to 100 ml. Formulations that have been made were stored in 10 ml closed vials. This formulation was terminally sterilized by autoclaving at 121°C for 15 min

Evaluation

- Organoleptic examination
- pH measurement
- Viscosity measurement
- Determination of chloramphenicol
- Compatibility study
- Sterility test
- Potential test

0.5 to 1g every 4-6 h.

2. Antipyretics

Example: Paracetamol

periods.

Indications : Mild to moderate pain including dysmenorrhoeal pain, headache pain relief osteoarthritis and soft tissue lesions, pyrexia including post-immunisation pyrexia acute migraine attack

Availability TABLETS 500 and 650 mg Plain, 750 mg DT

SYRUPS/SUSPENSION 125 and 250 mg/5ml: INJECTION 2 ml ampoule 125 mg/ml; Intravenous infusion 500 mg and 1g.

Dose Oral: Adult-0.5 to 1g every 4 to 6 h

indigestion

Child- for post-immunisation pyrexia, up to 2 months: 60 mg . 3 month to 1 year- 60 to 120 mg every 4 to 6h. 1 to 5 years : 120 to 250 mg every 4 to 6 h. 6 to 12 years: 250 to 500 mg every 4 to 6h

liver failure. kidney failure

Precautions Hepatic impairment, renal impairment; alcohol dependence, lactation; pregnancy, overdosage; interactions; G-6-PD deficiency.

Adverse Effects Rare but rashes and blood disorders reported; important: liver damage (and less frequently renal damage) following overdosage; dyspepsia.

Storage Store protected from light and moisture.

Material and Methods

- **Material**
- Paracetamol (Acetaminophen) was taken as API (Active Pharmaceutical Ingredient).
- Coconut Oil was used as a binder; lubricant used was Magnesium Stearate, and starch.
- Talc and Starch (dry) were used as disintegrants and glidant.
- A solution of 0.1 N HCl was used for disintegration and dissolution All the chemicals and reagents were of analytical grade.
- The paracetamol stock solution and standard solutions were prepared as mentioned in Indian Pharmacopoeia.

- **Preparation of tablets**

1. Paracetamol tablets contain 500 mg of paracetamol were prepared using three different concentration of coconut oil (binder).
2. A 500 mg of Paracetamol (API) was weighed accurately along with 2 gm of starch, 3.6 gm of talc and 0.6 gm of magnesium stearate. All the ingredients were transferred to mortar pestle and were mixed until properly blended.
3. The composition of paracetamol tablets is given in Table 1. Then, 2 ml (1%) coconut oil was added to the blended mixture of powder and again mixture was being triturated for about 5 minutes.
4. The powder was then passed through sieve no. 25 to prepare small granules. The granules were then dried at 60 °C for about 1hour in hot air oven and screened through No 24 mesh.
5. Similarly, 4 ml (2%) and 6 ml (3%) of coconut oil was used as binder and same procedure was carried out for the other two batches. The resulting mixture was compressed using tablet Compression Machine.
6. About 20 Tablets were prepared for each formulation i.e., for each concentration of coconut oil (1%, 2%, 3%). The compressed tablets of each batch were stored in proper containers at room temperature.
7. Such method of tablet production has previously been described by several authors who provided reproducible experimental results in terms of *in vitro* release.

Table 1: Composition of paracetamol tablets

Ingredients	Batch (A1)	Batch (A2)	Batch (A3)
Paracetamol	500 mg	500 mg	500 mg
Corn Starch	2 gm	2 gm	2 gm
Coconut Oil	2 ml	4 ml	6 ml
Magnesium Stearate	0.6 gm	0.6 gm	0.6 gm
Talc	3.6 gm	3.6 gm	3.6 gm

Evaluation of tablets

Pre-compressional parameters were studied like the angle of response, bulk density, tapped density, compressibility indices etc Hausner ratio.

Dose. oral ~~adult~~: 10 to 60mg/day. single dose or in divided 2 to 4 doses.
Low :- 2.5 to 10mg/day
High :- 1 to 1.5mg/day/kg.

3. Steroids

Example; Hydrocortisone , Prednisolone

- Corticosteroid include hormones secreted by the adrenal cortex and synthetic analogues of these hormones. Pharmacology of the corticosteroids is complex and their action are wide ranging . In physiological (low) doses they replace deficient endogenous hormones. In pharmacological (high) doses glucorticoids decrease inflammation and suppress the immune response.
- **Indications:** Adrenocortical insufficiency , hypersensitivity reactions including anaphylactic shock ; inflammatory bowel disease asthma perineal trauma joint inflammation seborrheic dermatitis. Adrenal gland absent on kidney Ulcer.
- **Avaliability tablets :** 5,10,20 mg Cream 10g(1% w/v) ointment 1%, 2.5% (w/v) injection 100,200,400mg vial (25mg/5ml)
- **Dose oral : Adult** 20 to 30 mg daily in divided doses (usually 20 mg in the morning and 10 mg in the evening)

Child 400 to 800 ug/kg/day in 2-3 divided doses

- **Precautions :** lactation and pregnancy

Material And Methods

- **Materials**

prednisolone IP, microcrystalline cellulose ,cross carmellose sodium, sodium starch glycollate, aerosil, isopropyl alcohol, talc, magnesium stearat e, Eudragit L100, Eudragit S 100, DEP, TIO

Method

1. Preparation of core tablets

- The core tablet of prednisolone 100 mg were prepared by direct compression method of manufacture using MCC (AVICEL) as the main constituent.
- Prednisolone, MCC, SSG, Cross carmellose sodium were passed through sieve no #40 and thoroughly mixed in a polythene bag (approx. 10 min).
- Loss on Drying (LOD) was measured by halogen moisture balance (Mettler Toledo).
- Above mixer was lubricated granules were lubricated with talc ,aerosil and Magnesium stearate which were already passed through sieve no # 60 and compressed in to tablets on a 35 station single rotary machine using 8/32 inch Stand ard concave, Plain/Plain punch.
- The compression pressure level was kept constant for al l the batches by adjusting the pressure control Known to the same settings.

2. Coating of the tablets

- It was done by using the standard coating pan, wher e fixed numbers of tablets were coated each time by atomizing the polymeric coating solution through the means of spray gun.
- The scale-up variables including pan loading, pan speed, number of spray guns, spray rate, and inlet airflow etc. Were considered.
- About 500 tablets of prednisolone tablet were taken and allow to coatings in pan coater at 30 rpm and 50°C temperature.
- Coating was carried out with spraying method and dried with same.

3. Evaluation of tablets

The prepared tablets were evaluated for the following parameters Hardness, measured by tablet hardness tester; (Kilo Pascal), Weight variation (Average weight of ten tablets by electronic weighing balance), Thickness which was measured by Vernier Caliper in millimeter (mm), Friability was checked by USP appa ratus (Roche friabilator) for 100 rpm. validation.

potential test, stability test, compatibility test.

4. Injectibles

Example: saline

- Solutions of electrolyte are given intravenously to meet normal fluid and electrolyte requirements or to replenish continuing losses when patient is nauseating or vomiting and is unable to take adequate amount by mouth.
- The nature and severity of the electrolyte imbalance must be assessed from the history and clinical , biochemical examination of each individual.
- Sodium chloride in isotonic solution provides the most important extracellular ions in near physiological concentration and is indicated in sodium depletion
- **Indications;** fluid and extracellular volume depletion with excess diuresis gastroenteritis
- **Avaliability injection :** 250,450,500ml and 1 L (Dextrose 5% and sodium chloride 0.9%)
- **Dose by intravenous infusion : Adult and child** determined on basis of clinical and wherever possible electrolyte monitoring.
- **Precautions :** restrict intake in impaired renal function,cardiac failure, hypertension
- **Adverse effect:** adminstration in high doses may give rise to edema
- **Storage :** store in a single dose container at a temperature not exceeding 30°C

Glucose Sodium Chloride.

Types of injectibles

- Perenteral preparations can be classified as follows:-

1. Solutions or emulsions of medicaments suitable for injections
2. Sterile solids
3. Sterile suspensions
4. Transfusion fluids

Formulation of injectibles

- The formulation of Injectable need carfeful planning, thorough knowledge of the medicaments and adjuvants to be used.
- The excess use of adjuvants in Injectable should be avoided as some of these may interfere with the drug.
- In the preparation of Injectable, the following substances are added to make a stable preparation:-

1. Vehicles
2. Adjuvant

(a) Solubilising agents
(b) Stabilizers
(c) Buffering agents
(d) Antibacterial agents
(e) Chelating agents
(f) Suspending, emulsifying and wetting agents
(g) Tonicity factors

General requirements for injectibles

- The formulation of parenteral products involves careful consideration of the following requirements:-

1. Stability
2. Sterility
3. Free from pyrogens
4. Free from foreing particles
5. Isotonicity
6. Specific gravity
7. Chemical purity

Processing of injectibles

- The following steps are involved in the processing of parenteral preparations:-

1. Cleaning of containers, closures and equipment
2. Collection of materials
3. Preparation of parenteral products
4. Filtration
5. Filling the preparation in final containers
6. Sealing the containers
7. Sterilization
8. Evaluation of parenteral preparations
9. Labelling and packaging

Evaluation of injectibles

- The finished parenteral products are subjected to the following test, in order to maintain quality control:-

1. Sterility test
2. Clarity test
3. Leakage test
4. Pyrogen test
5. Assay

Labelling

- After evaluation of the parenteral preparation, the ampoules, via and transfusion bottles are properly labelled and packed.

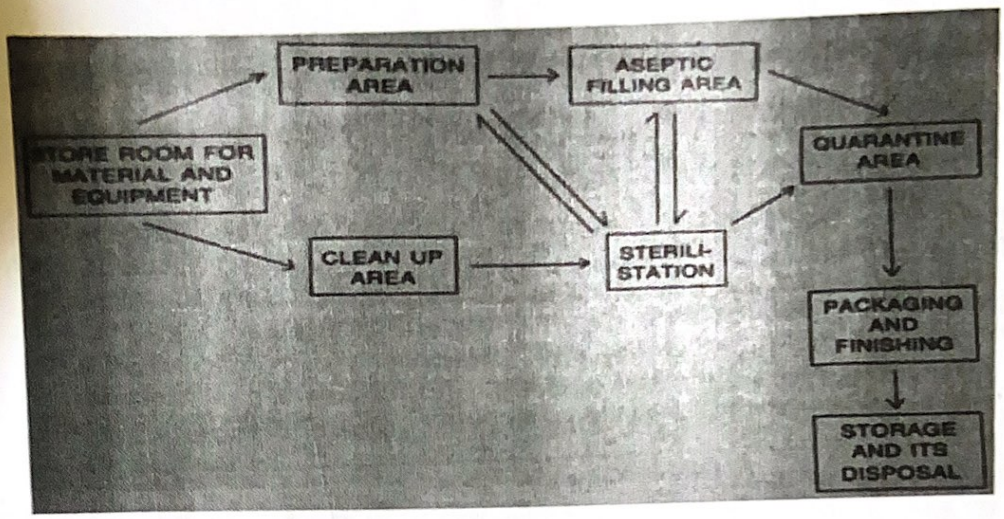
- **The label should state:-**

1. Name of the preparation
2. Quantity of the preparation
3. Mfg. Lic. No.
4. Batch No.
5. Date of manufacture
6. Date of expiry
7. Storage conditions
8. Retail price
9. Manufacture's address

Packaging

- Parenteral packaging includes ampoules, rubber stoppered vials and bottles, plastic bags and bottles, glass and plastic syringes, and syringe-vial combinations.
- Glass containers have traditionally achieved widespread acceptability for parenteral products because of their relative inertness.
- In recent years, hospital preference for unit-dose and clinical convenience has resulted in an increase in products packaged in disposable syringes and the development of polyvinylchloride, polyester, and polyolefin plastic containers for IV fluids.

Flowchart of parental product preparation



5. Vitamine

Example: Vit C

- Ascorbic acid (Vit C) Pregnancy category - A, C.
- **Indications;** prevention and treatment of scurvy
- **Availability tablets** 100 and 500 mg Drop 100mg/ml Injection 5ml ampoule (100mg/ml)
- **Dose oral : Adult and child** for Prophylaxis of scurvy 25 to 75 mg daily and for treatment of scurvy 0.5to 1.5g / day
- **Precautions :** Acetylsalicylic acid hypersensitivity,pregnancy etc
- **Adverse effect:** gastrointestinal disturbance reported in large doses
- **Storage ;** Store protected from light and moisture . Avoid contact with metals.

Material and Methods

- **Requirements**:Ascorbic acid, Thiamine Hydrochloride, Riboflavin and Nicotinamide
- **Method**

1. All powder compounds were accurately weighted, passed through a standard sieve (sieve no 80) and thoroughly blended for 5 min.
2. After being mixed powders were evaluated for bulk density and tapped density, compressibility index (Carr's index), Housner ratio and angle of repose.
3. Chewable tablets were prepared by direct compression using rotary tablet compression machine.
4. Six batches (F1, F2, F3, F4, F5, and F6) of white-yellowish tablets with an average mass of 500 mg were obtained.
5. Completed composition of the tablets of six batches

Final composition

Table 1: Final composition of chewable tablet formulation (F4)

Ingredients	Amounts	
	mg	%
Ascorbic Acid	50	10
Riboflavin	2	0.4
Nicotinamide	20	4
Thiamine HCL	2	0.4
Zinc Sulphate	15	3
Magnesium Oxide	60	12
Copper Sulphate	2	0.4
Folic Acid	4	0.8
Starch	40	8
Manitol	100	20
Sucrose	194	38.8
Magnesium Stearate	5	1
Talc	5	1
Vanilla Powder	1	0.2
Total	500	100

Evaluation of Tablets

Pre-compressional studies of powder blend

- In the development of new dosage form, the pre-formulation study is the prior step in the potential drug development.
- It is the principal investigation in the drug development to obtained information on the known properties of the compound and the proposed development schedule.
- So, this pre-formulation investigation may merely confirm that there are no significant barriers to compound development
- pre-compressional parameters were studied like the angle of repose, bulk density, tapped density, compressibility indices et

Result

The chewable multivitamin tablet of was formulated by direct compression method. This technique was used for a tablet which minimise processing steps and eliminated wetting and drying process.

Credit 3.0

Regulatory authorities and its role

FDA The Food and Drug Administration is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation.

FDA also has responsibility for regulating the manufacturing, marketing, and distribution of tobacco products to protect the public health and to reduce tobacco use by minors.
people

FDA is responsible for advancing the public health by helping to speed innovations that make medical products more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medical products and foods to maintain and improve their health.

boost.
~~increase~~.

FDA fulfills this responsibility by ensuring the security of the food supply and by ~~fostering~~ development of medical products to respond to ~~deliberate~~ and ~~naturally~~ ~~emerging~~ public health ~~threats.~~
improve.

Encouraging stepwise clinical development;

~ Having proper controls in registrational trials, often best achieved through use of randomization;

~ Properly addressing multiplicity through pre-specification of primary and secondary outcome measures and primary methods of analysis;

Primary methods are analysis. → Recognise the value of outcome.
→ Guiding proper design of trials → Clinical ~~the~~ trial assuring
→ Enhansing the trial product → Recognise exploratory analysis.
→ Recognise need of confirmat' trial → Important safety signals has beed identify.

~ Recognizing reliability and interpretability of efficacy is enhanced by assessing effects on direct measures of how a subject "feels, functions or survives," and recognizing the likelihood of being misled when relying on replacement endpoints such as biomarkers that have simply been shown to be correlated with direct measures of tangible benefit and often do not capture risks adequately;

~ Recognizing the value of blinding when outcome measures are subjective;

~ Guiding proper designs of non-inferiority trials;

~ Ensuring clinical trials are designed and conducted in a manner to assure the safety and ethical protection of study participants;

~ Enhancing the quality of trial conduct by encouraging timely enrollment, best real-world achievable adherence to experimental and control regimens, pro-active efforts to maximize retention, and maintaining confidentiality of efficacy data in ongoing trials;

~ Recognizing that exploratory analyses usually should be viewed as generating hypotheses; and

~ Recognizing the need for confirmatory trials, especially in settings where positive predictive probabilities for efficacy are not strong (such as when obtaining marginally positive results in a setting where the pre-trial likelihood of meaningful benefit was rather low), or when *post hoc* analyses would properly be viewed as being hypothesis generating, or when important safety signals have been identified.

Regulatory programs

Emergency approvals (EUA)

(EUA)

Emergency Use Authorization (EUA) is a mechanism that was created to facilitate the availability and use of medical counter measures, including vaccines, during public health emergencies such as the current COVID-19 pandemic.

Regulations

The programs for safety regulation vary widely by the type of product, its potential risks, and the regulatory powers granted to the agency. For example, the FDA regulates almost every facet of prescription drugs, including testing, manufacturing, labeling, advertising, marketing, efficacy, and safety—yet FDA regulation of cosmetics focuses primarily on labeling and safety.

In general, FDA regulates:

Foods, including:

- dietary supplements
- bottled water
- food additives
- infant formulas
- other food products (although the U.S. Department of Agriculture plays a lead role in regulating aspects of some meat, poultry, and egg products)

Drugs, including:

- prescription drugs (both brand-name and generic)
- non-prescription (over-the-counter) drugs

Biologics, including:

- vaccines for humans
- blood and blood products
- cellular and gene therapy products
- tissue and tissue products
- allergenics

Medical Devices, including:

- simple items like tongue depressors and bedpans
- complex technologies such as heart pacemakers
- dental devices
- surgical implants and prosthetics

Electronic Products that give off radiation, including:

- microwave ovens
- x-ray equipment
- laser products
- ultrasonic therapy equipment
- mercury vapor lamps

- sunlamps

Cosmetics, including:

- color additives found in makeup and other personal care products
- skin moisturizers and cleansers
- nail polish and perfume

Veterinary Products, including:

- livestock feeds
- pet foods
- veterinary drugs and devices

Tobacco Products, including:

- cigarettes
- cigarette tobacco
- roll-your-own tobacco Weed.
- smokeless tobacco

WHO: The World Health Organization (WHO) is a specialized agency of the United Nations responsible for international public health. The WHO Constitution, which establishes the

agency's governing structure and principles, states its main objective as "the attainment by all peoples of the highest possible level of health." It is headquartered in Geneva, Switzerland. As World War II was winding down, countries came together to form the United Nations and voted to create a global health agency as a U.N. arm. And so in 1948 the World Health Organization was founded for "the attainment by all peoples of the highest possible level of health." As a specialized agency of the U.N., WHO has as its directive "to act as the directing and coordinating authority on international health work," according to the agency's constitution.

WHO replaced several regional health authorities that had been established in Europe and the Americas in the early 1900s to help prevent the spread of diseases such as smallpox and typhus. WHO started with 55 member states and has now grown to include 194 member states and two associate members (Puerto Rico and Tokelau).

The WHO has played a leading role in several public health achievements, most notably the eradication of smallpox, the near-eradication of polio, and the development of an Ebola vaccine. Its current priorities include communicable diseases, particularly HIV/AIDS, Ebola, COVID-19, malaria and tuberculosis; non-communicable diseases such as heart disease and cancer; healthy diet, nutrition, and food security; occupational health; and substance abuse.

WHO's mission: the organization's overarching mission: "The mandate we have [is] to establish global standards and to give strong advice to countries regarding rational public health measures."

To achieve these goals, WHO does not typically give out grants or loans or send doctors and others from its staff to countries to provide hands-on medical treatments. Rather, "what it does do is get

They

on the ground to provide direction, advice, help trace disease outbreaks and provide additional support when needed,"

CLSI:

The Clinical and Laboratory Standards Institute (CLSI) was founded nearly 50 years ago by clinicians and laboratory scientists as a not-for-profit standards development organization with the intention to work collaboratively on ways to ensure the quality of laboratory testing, improve patient care, and develop a formal consensus process for standardization in the field of laboratory medicine.

CLSI's mission continues to be to "develop clinical and laboratory practices and promote their use worldwide." CLSI supports a global community of more than 1700 institutional and organizational members from 68 countries, including hospitals, universities, professional societies, diagnostic companies, and government agencies, as well as individual members.

CLSI actively promotes global harmonization of standards through its own initiatives and through communication and cooperation with many organizations around the world, such as WHO, the College of American Pathologists (CAP), the CDC, the US Food and Drug Administration (FDA), the International Organization for Standardization (ISO), the Kenya Accreditation Service (KENAS), the South African National Accreditation System (SANAS), and others. CLSI's active collaboration with such organizations results in laboratory standards recognized by these organizations and broadly accepted in the international clinical laboratory community.

CLSI facilitate the creation of best practice standards, guidelines, and products for medical laboratories. Organizations use CLSI standards to improve their testing outcomes, maintain

- The first role of CLSI is setting guideline for quality of medicinal laboratory testing.
- It helps in developing standard reference method for various laboratory tests.
- Providing quality control parameters for standard test method.
- Establishing interpretative criteria for results of standard laboratory tests.

quality
accreditation, bring products to market faster, and navigate regulatory hurdles. Our products focus on the following specialty areas:

- Automation and Informatics
- Clinical Chemistry and Toxicology
- General Laboratory
- Hematology
- Immunology and Ligand Assay
- Method Evaluation
- Microbiology
- Molecular diagnostics
- Newborn Screening
- Point-of-Care Testing
- Quality Management Systems
- Veterinary Medicine