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A REVIEW: ROUTES OF DRUG ADMINISTRATION WITH THEIR RECENT ADVANCES

[1]Mrs. Aishwarya P Pimple, [2]Miss. Varsha S Kudal, [3]Dr. Gajanan S Sanap, [4]Miss Pooja S Murkute
[1]Assistant Professor, [2]Student, [3]Principal, [4]Assistant Professor
[1]Quality Assurance
[1]Late Bhagirathi Yashwantrao Pathrikar College of Pharmacy (D and B Pharmacy), Pathri, Aurangabad, Maharashtra, India

***Abstract*:** This review article shows the diverse routes of administration of different drug. In pharmacology, the route of administration is the pathway by which the medicine is transfer into the body for the treatment of several diseases or disorders. The Bioavailability of the effective drug present in the body is influenced by the various methods of administration. This article contains the classification of routes of administration with their salient features, advantages, disadvantages and examples. The most recent inventions in drug preparations delivered through these routes have also been discussed.

***Keywords*:** Route, Administration, Drug, Systemic, Oral, Sublingual, Rectal, Parenteral, Intravenous, Intramuscular, Subcutaneous, Intra-arterial, Intra-articular, Intra-thecal, Intradermal, Inhalational, Transdermal, Local.

Introduction:

Routes of administration: In pharmacy, a route of administration is the pathway through which a medication, fluid or different substances is taken or injected inside the body. [[1]]

Classification:

The routes of administrations are divided into several classes:

1. Systemic Route:

Table No 1: Classification of Systemic Route

Enteral Route:	Parenteral Route:
Oral Sublingual Rectal	Inhalational Transdermal Injections: Intravenous, Intramuscular, Subcutaneous, Intra-arterial, Intra-articular, Intrathecal, Intradermal.

2. Local Route:

1) Systemic Route:

Systemic administration occurs when medication, nutrition or a different substance is injected into the vascular system and affects the complete body. During this route drug reaches direct into the circulation, therefore it is known as systemic route. During this route, introduction of drug can take place through enteral administration (absorption of the medicine through the GI-tract) or through parenteral administration, which are both options for this route (generally injection, infusion or implantation). [[1],[4]]

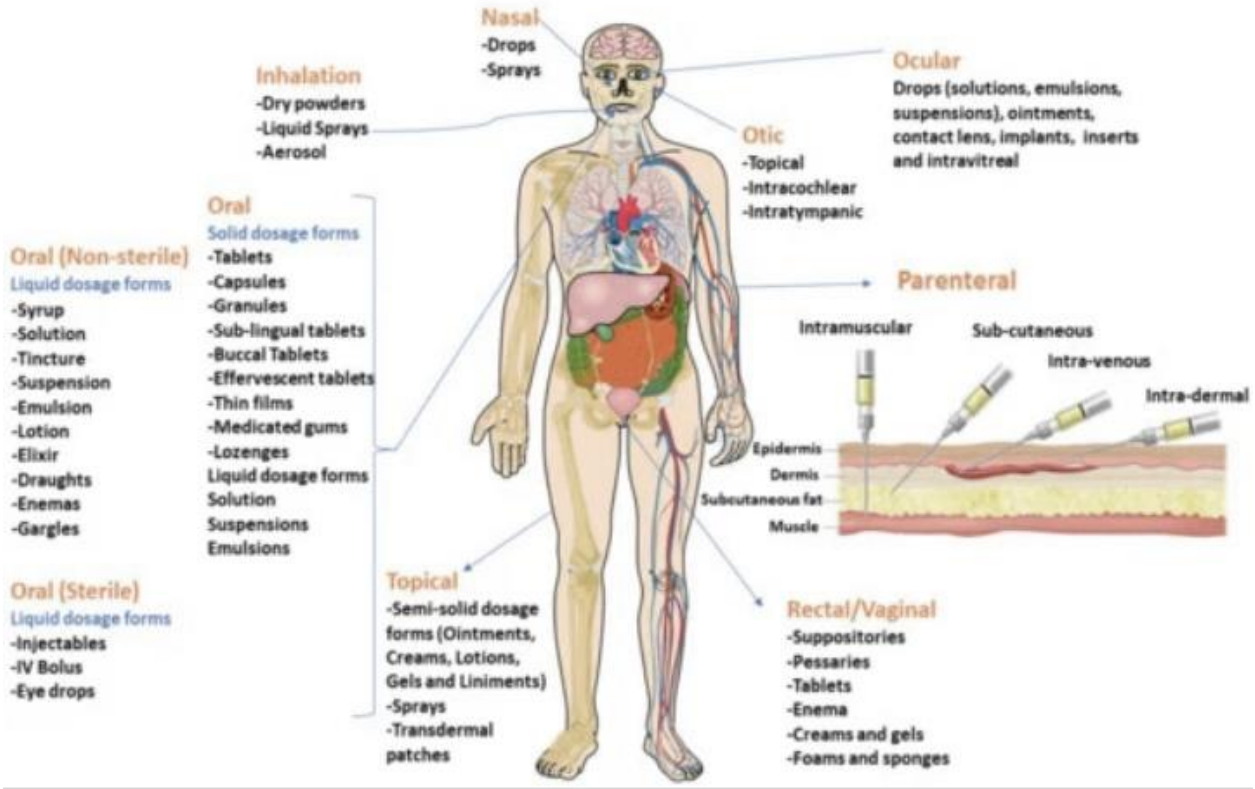

Fig 1: Types of Routes of Administration

The systemic route is divided into two categories:-

Enteral Route: When a medicine is administered by enteral route, it is deposited into the gastrointestinal tract and reaches inside the bloodstream. Enteral administration includes the esophagus (or gullet), stomach and intestines (both small and large). It is again divided into 3 categories.

Oral Route: Because of its benefits such as patient comforts and drug delivery convenience and non-invasiveness the oral path is the most precious route. About 60% of existing small-molecule drug products are administered orally. According to current estimates, oral formulations are meant for human use. [[5]] In oral route, the drug is swallowed and taken orally. It is also known per oral (p.o). [[3]]

Advantages:

1) It is convenient, can be self-administered, easy to take, inexpensive and pain free.
2) No sterile precautions required.
3) It is not required special data or supplies (syringes, needles) for its use.
4) The total length of GI tract is used for absorption.
5) By using this route both solid and fluid dosage forms can be administered.

Disadvantages:

1) It shows slow onset of action, hence unsuitable for use in emergency.
2) It requires patient co-operation or compliance.
3) It is able to only use in aware patients and those patients who can consume.
4) It is unsuitable for:-

a) Highly irritating and unpalatable medications.
b) Unabsorbable drugs (ex. Amino glycosides).
c) Drugs that are degraded by digestive juices (ex. Insulin)
d) Drugs that have a broad first pass degradation (ex. Lidocaine).
e) Patient with sever vomiting and diarrhea.

5) Sometimes inefficient – only fraction of the medication may be absorbed.

First - Pass Effect: It is a term in which a medication gets digested at a particular location within the body system, ensuing in a low concentration of the effective medication when it reaches its site of operation or the systemic circulation. The liver is the main site of drug metabolism, but the first-pass effect can also happen in the lungs, GIT, vasculature, and another metabolically reactive tissue in the body. [[8], 430] This is the action that obtained when medications are taken by mouth. When medicinal agent is absorbed from the gut and transferred to the hepatic system via portal circulation, it is known to as first-pass metabolism. When the mediator is transferred orally, the greater the first pass effect, the less the agent will enter the systemic circulation. [[2], [10]].

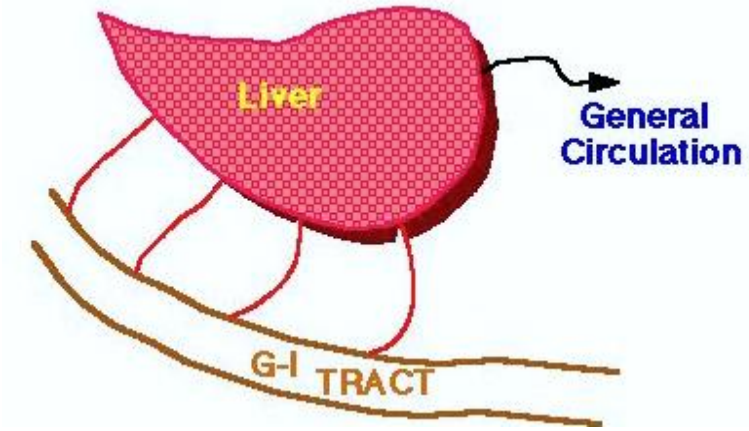

Fig 2: First Pass Effect

Ex. of Drugs that have a strong first pass effect: Lidocaine, Diazepam, Propranolol, Imipramine and Midazolam.
Ex. of dosage form used by the oral path include: Tablet, Capsules, Suspensions, Syrups, Elixir, Emulsions, etc.
Sublingual and Buccal Route:

Sublingual Route: Sublingual delivery happens through the mucosa of the ventral plane of the tongue it deteriorating there and also the absorption happens in mouth (i.e. the medication is kept under the tongue). Mucin, a main component of the mucus layer on the mucosal surface, is produced by salivary glands, which help in saliva production and secretion. Saliva is necessary to lubricate and moisten the mucosae, as well as to aid the masticatory method by joining the food bolus prior to and during consuming. [[11]]

Buccal Route: The administration of the preferred medication through the oral mucosal film coating of the oral cavity is known as buccal drug delivery. In this path the drug is retained in the oral cavity (between the gums and cheek) where it break down and absorbed in the mouth. [[12]]

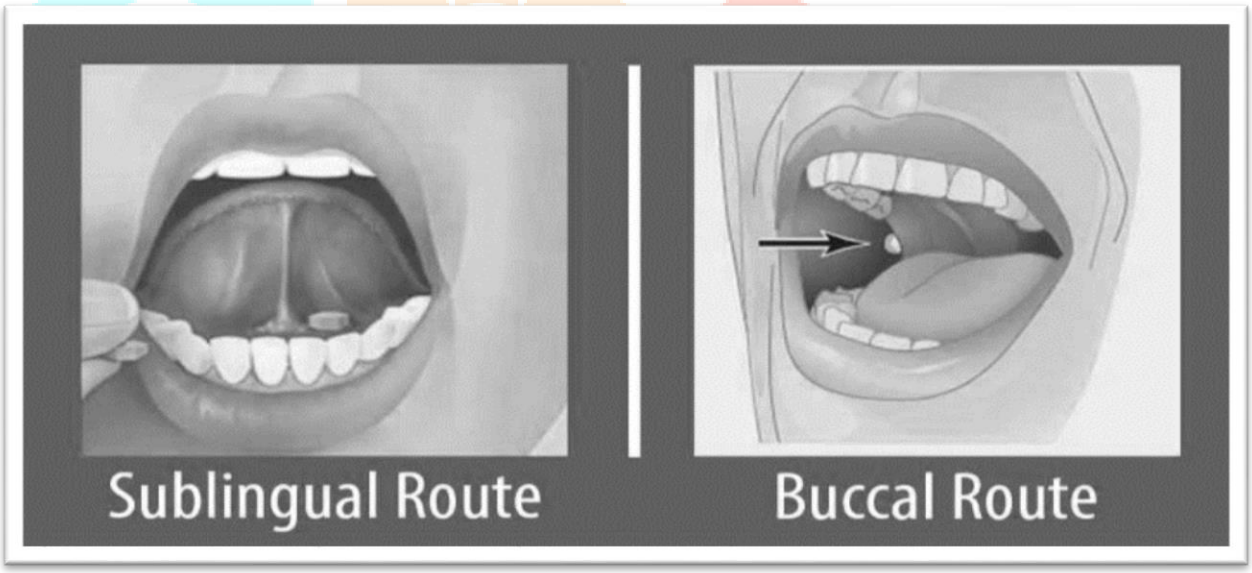

Fig 3: Sublingual and Buccal Routes

Advantages: [[13], [14]]
Advantages of both sublingual route and buccal route:
1) Bypassing the first-pass metabolism.
2) Increased bioavailability and self-administrable.
3) It quickly dissolves in the mouth, allowing for rapid absorption.
4) Because the drug does not exceed through the stomach, it is not degraded by the enzymes and acids existing in the stomach, therefore it is remain stable.
5) Shows quick onset of effect.
6) By throwing out the tablet, the action can be terminated.
Disadvantages: [[13], [14]]
Disadvantages of both sublingual route and buccal route:
1) Bitter and irritating drugs are not suitable.
2) Highly ionic medications cannot be administered
3) High doses can't be taken.
4) Less patient compliance.
5) The medicine must be small size in order to stay in the mouth.
Examples of sublingual route tablets: Nitroglycerin, Mirtazapine, Rizatriptan.
Examples of buccal route tablets: Danazol, Metronidazole.

Rectum Route: The ending portion of the large intestine is the rectum contains a length of about 10 to 15cm and a diameter of 15 to 35cm. [[15]] Several medications that are taken by mouth can also be taken rectally as s suppository. When a medicine is fused with a waxy material and injected into the rectum, it dissolves or liquefies. Drug is easily absorbed because the rectums wall is slim and its blood provides a rich contains. [[3]]

Advantages: [[15]]

1) It avoids the first-pass metabolism, suitable for children and old age and used for unconscious and vomiting patients.
2) Irritating drugs are contraindicated.
3) The rate of medication absorption is not influenced by food or the gastric emptying rate.
4) Drugs are protected from degradation by avoiding contact with digestive juices in the upper gastrointestinal tract.

Disadvantages: [[15]]

1) The rectum's absorbing surface part is minor than that of the duodenum.
2) The rectum's fluid content is lower than that of the duodenum, which may cause dissolving issues with certain medicines.
3) The micro-organism in the rectum causes degradation of some drugs.
4) Defecation can cause absorption to be disrupted, which may happen especially when the drug is irritating.

Table No 2: Examples of rectal formulations medically approved for local absorption: [[16]]

Medication/Drug	Brand Name	Suggestion	Dosage System
Glycerol	glycerol	constipation	suppository
Bisacodyl	dulcolax bisalax	constipation	suppository Enema
Prednisolone	colifoam	anti-inflammatory	rectal Foam
Budesonide	budenofalk	anti-inflammatory	rectal Foam

Table No 3: Examples of rectal formulations medically approved for systemic absorption: [[16]]

Medication/Drug	Brand Name	Suggestion	Dosage System
Ondansetron	zofran	vomiting and nausea	Suppository
Ibuprofen	nurofen	pain, fever	Suppository
Diclofenac	voltaren	pain, fever	Suppository
Indomethacin	indocin	pain	Suppository

There are two rectal routes:-

1) Vaginal Route: The vagina is commonly a perfect way for drug administration as it permits for the introduction of lower doses, steady drug levels and fewer common administration than the oral route. Before 1918, the vagina was thought to be organ that was unable of absorption of morphine, atropine and potassium iodide following vaginal administration. [[17]]This route is also used to given estrogen to women going through menopause, because the medicine helps preventing thinning of the vaginal wall, an effect of menopause. [[18]]

Advantages:-

1) One of the important benefits of vaginal administration over oral inoculation is that drugs ignore gastrointestinal absorption and the hepatic first pass effect. [[19]]
2) It control the inconvenience caused by pain, tissue injure and probable infection by other parenteral route.
3) The self-incorporation and eliminate of the dosage form is possible. [[20]]

Disadvantages:-

1) It may produce local irritation in some cases.
2) This route is for females only.
3) There may be significant variation in the speed and amount of drug absorption.

Table No 4: Compounds being clinically examined for administration via the vagina.

Drugs	Use Being Examination
Glyminox gel[[21]]	Inhibition of sexually transmitted diseases, Contraception,
Terbutaline vaginal gel[[22]]	Dysmenorrhea, Endometriosis
Demegen gel[[23]]	Prevention of sexually transmitted diseases
Oxybutynin vaginal gel[[24]]	Overactive bladder

Urethral Route: The urethra is used to deliver some drugs. This route is known as urethral path of drug administration.

Advantages:-

1) Used in patient who having nausea and vomiting,
2) Minimum or no first pass effect.
3) Higher concentrations quickly achieved.
4) Used in unaware patients and children.

Disadvantages:-

1) It is inconvenient and may cause irritation.
2) Absorption may be variable, slow and erratic.
3) Infection of rectal mucosa can occur.

Examples: Urethral Bogies and alprostadil urethral suppository is working to take care of men who have Erectile Dysfunction (also known as sexual impotence). [[25]]

Parenteral Route: The word parenteral is derived from the two words 'Para' meaning beyond and 'Enteral' meaning intestine, it means to avoid the intestine. [[26]] According to the USP24/NF19 parenteral articles are defined 'as those preparations planned for inoculation through the skin / instead of passing through the GI tract, active chemicals can be delivered directly to a blood vessel, body part, tissue or lesion. [[27]] Patients who are admitted and who are in bed rest are completely reliant on parenteral nutrition includes fluids, electrolytes or supplements through parenteral route. [[26]]

Advantages:-

1) It provide fast onset of action and can be administered accurate dose.
2) Medications that have low absorption in the digestive tract and drugs like insulin which are unsteady in the GIT track can easily be administered by this route.
3) It minimizes the first pass effect and provides more bioavailability.
4) Unconscious, uncooperative and vomiting patients can be easily dealt with.
5) It is the best reliable route in case of emergencies since the medicine is administration faster leading to a more efficient action. [[28]]

Disadvantages: - [[29]]

1) It should be administered aseptically.
2) It provides pain or injury at the site of injection.
3) The administration of drug through wrong route may provide serious effect.
4) Self-administration is not possible.
5) There are greater chances of injury to the local tissue.

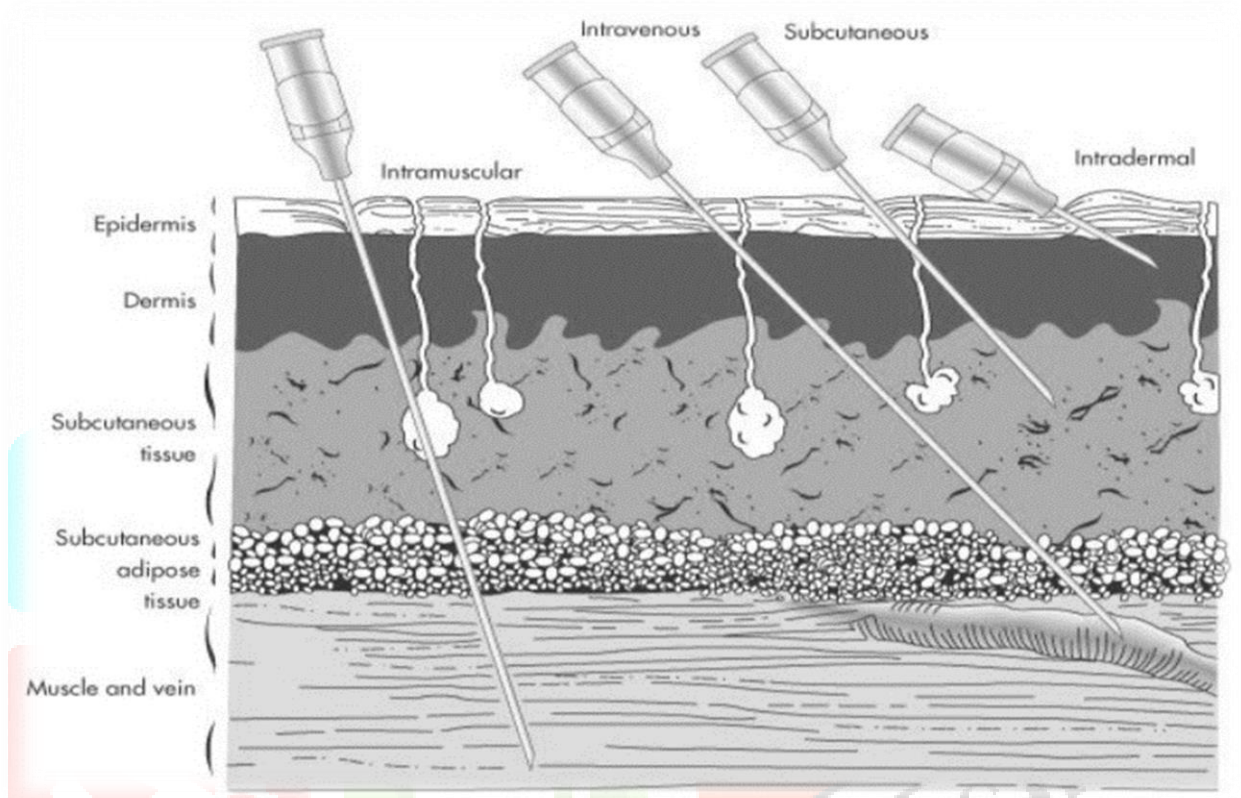

Fig 4: Different Types of Parenteral Routes

By using injection parenteral route divided as follows:-

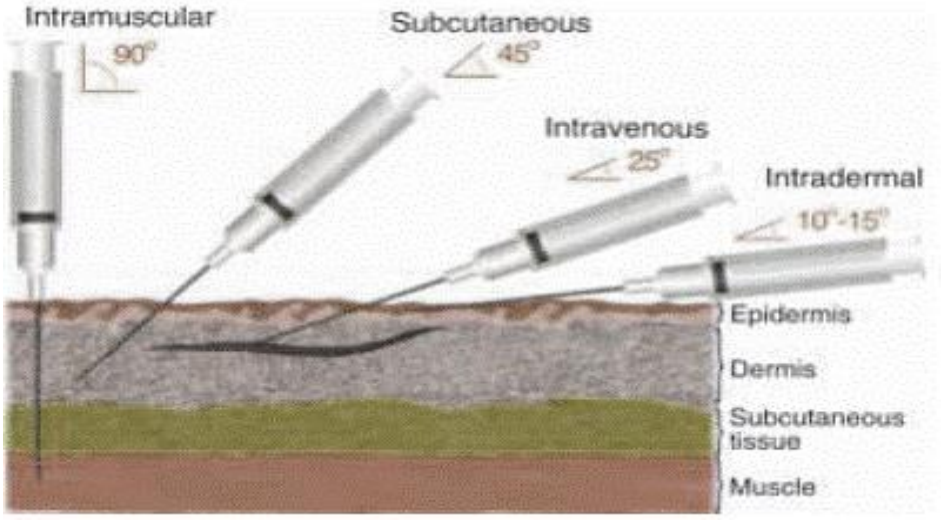

Fig 5: Angle of Injections of Different types of Parenteral Routes

Intravenous (IV): IV route involves the transferred of a drug solution through a needle, directly into a vein. In this route, the medicine is injected within the vein lumen, mostly the antecubital vein (superficial veins) in the system of a bolus or as an infusion. [[29]] The bolus injection causes a very high drug concentration firstly in the right chambers of the heart and then to the lungs. Then this high concentration enters the circulation. However, during this case, the peak amount reached by the administered drug significantly dependent highly on the speed at which the drug is injected. The intravenous infusion is a preferred process than the bolus administration as it avoids the a) ambiguity in absorption of the medication from other areas and b) the elevated plasma concentration that occurs due to a bolus injection. [[30]] It is the commonly used method of administration. [[28]]

Advantages: [[28], [29], [10]]

1) Bioavailability is 100% and drug bypasses first pass metabolism.
2) Drug enters the bloodstream immediately having full access to the complete body hence rapid action is produced and making this method the most effective in an emergency.
3) Because the venous tissue layer is insensitive, drugs that cause severe irritation can be given because the blood dilutes the drug moiety.
4) Drug dose titration is possible in a condition where the drug has a short duration of action and the response can be measured exactly.
5) Very lesser dose is required &medications can be delivered at uniform rate.
6) Hypertonic solutions can also be taken together with GIT irritation causing medicines.

Disadvantages:-

1) This method has a high chance of bacterial contamination.
2) If the medication administrations attend extravasation, then thrombophlebitis and venous thrombosis of the vein in which drug is transferred and necrosis of the tissues nearby that specific vein can occur.
3) As the essential organs of the body like heart and lungs get exposed to a high drug concentration, thus, this path has the maximum risk factors.
4) Only fluid solutions of the drug can be administered, suspensions cannot administer.
5) Depot preparations i.e. aqueous suspensions and oily solutions for this method cannot be made.

Examples of Intravenous Drugs: [[30], [10]]

1) Propofol (an anesthetic).
2) Diazepam (for treatment of status epilepticus).
3) Glucose, saline glucose and many antibiotics.

Intramuscular Route: In this path the drug is inserted into the muscles (Large muscles like deltoid, gluteus maximus, triceps and rectus femoris) with the aid of injection. This allows the rapid absorption of the medicine into the bloodstream. Drugs once attain to the muscles then absorbs into the blood. [[3]]

Advantages:

1) As then muscles have less sensory nerves ending in them, so medicines that cause minor irritation can be administered.
2) Absorption is faster as the muscular area is vascular.
3) The GI tract and first pass degradation is avoided.
4) Unlike the i.v. preparations, depot preparations (ex. a suspension of the medicine made in a vehicle which is non-aqueous like PEG) of this path can be made and therefore sustained drug effects can be attained.
5) This method causes fewer pains then the i.v. method.

Disadvantages:

1) Injections can be painful and self-administration is difficult.
2) It break skin barrier and can produce anxiety.
3) Rarely, abscesses can form at the place of injection.
4) Local hematoma can develop in patients taking anticoagulant drugs; care should be taken before an i.m. injection.
5) Site complications.

Examples of intramuscular drugs: Narcotic, Antibiotic, Anti-emetics medications.

Subcutaneous Route: In this method of administration the medicine is injected below the skin into the adipose layer beneath the dermis, therefore it is also called as hypodermic administration. [[13]]The subcutaneous route is quicker than the oral path. But, they poses a limitation as the speed of absorption to an extent depends upon the position where the medicine is administered and the local flow of the blood on this place. [[30]]

Advantages: [[28], [29], [30]]

1) Easy absorption over a long phase of time.
2) Reduced risk as compared to i.v.
3) No help is necessary as the injection not be penetrated deeply.
4) Depot preparations for sustained action can be created.

Disadvantages: [[29], [10]]

1) Because the tissue is fewer vascular, moderate rate of drug incorporation is there as compared to i.v. and i.m. route.
2) The position of injection is abundantly supplied with nerves hence, drugs causing impatience can't be administered by this path because it may result in sloughing and necrosis.
3) Like to the intramuscular route, only lesser volumes can be administered.

Special forms of subcutaneous route: [[29]]

1) Dermojet: During this technique the drug is projected from an especially small pore using a gun like instrument. It is a painless method and is useful for mass inoculations.
2) Implantation of pellets: The drug is incorporated in the form of solid pellets and is located beneath the skin for sustained discharge over a long period of time.
3) Non-biodegradable and biodegradable implants: In this method, the crystalline drug is integrated in tubes or capsules and planted under the skin just like the pellets. The non-biodegradable once has to be detached after some times but biodegradable implants don't pose this problem. [[29]]

Subcutaneous injections are highly efficient in administering medications such as hypoglycemic agent (insulin), morphine, heroin and goserelin. [[1]]

Intra-arterial route: Intra-arterial medicine injection or infusion is a technique of transporting a drug directly into artery or arteries to localize its special effects to a specific organ/body region, where as reducing the introduction of the body to potentially harmful effects of the agent. This method is considered more risky than intravenous administration and should be reserved to specialists. [[32]]

Advantages: [[33]]

1) The first-pass effects are bypassed & bioavailability is 100 percent.

2) It is of excessive scientific value in injecting anticancer drugs, for ex. in limb malignancies, the drug is inserted into the brachial artery or femoral artery. Example: antineoplastic injected within the nearby of the tumor with a reduce of systemic adverse effects.

Disadvantages: [[33]]

1) Intra-arterial injection requires great skill and experience.
2) If the medicine is of unfavorable effect there could be great danger.

Intra-articular Route: In this path of injection, the medicine is given into the joint space. Intra-articular injections are 1 technique that physicians could use to heal joint pain. Corticosteroids were the first substances to be injected on a regular basis into the intra-articular space. [[31]]

Advantages: [[36]]

1) It offers direct access to the joint space, so increasing the bioavailability of therapeutic agents at the affected site whereas reducing systemic exposure, potential side effects and overall cost.

2) Intra-articular injections are normally considered safe; their therapeutic effectiveness remains severely limited due to rapid clearance of the drug.

3) Intra-articular injections are routinely used for various rheumatic diseases, particularly osteoarthritis.

Disadvantages:-

1) Strict sterile protection should be taken.
2) Frequent administration may cause injury to the articular cartilage.

Example: Hydrocortisone injection is use for rheumatoid arthritis, hyaluronic acid, local anesthetics & botox, etc. [31]

Intrathecal Route: This route includes the insertion of the drug into the sub-arachnoid space i.e. the CSF (cerebrospinal fluid) through a lumbar puncture needle. [[10]]

Advantages: [[37]]

1) High accessibility of the medication in the CSF because the BBB and blood CSF barrier is bypassed. Therefore the drug takes action directly on the CNS.
2) It is well-known in anesthesia and pain management.

Disadvantages:-

1) This injection requires great skill and extreme sterile conditions.
2) It is hurting and unsafe procedure

Examples: Xylocaine injection for anaesthesia of the spine, radiopaque media for visualization for the spinal cord, [[10]] Methotrexate for leukemia treatment to avoid CNS relapse, bupivacaine for regional anesthesia, baclofen for muscle spasm treatment. [[30]]

Intradermal Route: [[38]] In this routes of administration, the intradermal injections are transferred into the dermis, or the skin layer below the epidermis (while is the superior skin layer). This route includes the scarring or multiple puncturing of the epidermis through a drug go down to administer the drug into the epidermis.

Advantages: Absorption is time consuming (this is benefit in testing for allergies).

Disadvantages: Quantity of drug administered must be small.

Examples: BCG vaccines (sensitivity & diagnostic tests.)

Transdermal Route: The word transdermal has been taken from the basis 'Trans' means through, across or beyond and 'Derma' means skin. [[38]] A some of drugs can be express such that a 'patch' consist of the drug is rubbed to the skin. The drug escapes out of the patch, throughout the skin at a prearranged and controlled rate, and into the capillary bed. The penetrated drug is transferred by blood streaming to the complete body lacking the first-pass metabolism. Transdermal patches have numerous layers, as follows:-

1) Innermost adhesive layer (generally with a priming dose): bind to the skin.
2) Rate- controlling micro-pore membrane: Management the speed of transfer to the surface of the skin.
3) Main medicine reservoir layer: Contains the effective drug to be delivered.
4) Other support film: An occlusive supporting layer.

The transdermal patches typically last for 1-3 days and sometimes even longer. The patches is applied any place over the body, chest, abdomen, upper arm, lower back, buttock or mastoid regions are favored. [[39], [40]]

Advantages: [[40], [41], [42]]

1) Transdermal delivery can increases the curative value of various drugs by escaping specific difficulties related to the drug. Example GI- irritation, low absorption, disintegration due to 'first-pass' effect and making of metabolites that cause side effects.
2) Provides smooth plasma amount of the dug without fluctuations, for a long period.
3) Self-administration is possible.
4) Patient compliance is superior as many patients choose transdermal patches to oral tablets of same drugs.
5) Drug ingestion can be end at any point by simply eliminating the transdermal patch.

Disadvantages: [[41], [43]]

1) The medicines and the adhesive in the patch preparation may cause rashes, local irritation, erythema or contact dermatitis.

2) Only lipophilic medicines will successfully transfer the stratum corneum and hence the drugs must have some wanted physicochemical properties for penetration.

3) Doses of only 5mg or fewer can be injected in a body.

4) High rate of product.

Examples of transdermal route drug: Testosterone, Nitroglycerin, Hyoscine, Clonidine and Nicotine.

Inhalation/ Inhalational route: In this path of administration, the drug is run to the respiratory tract. Inhalation therapy is the top choice for respiratory organ diseases like asthma, cystic fibrosis and COPD (chronic obstructive pulmonary disease). [[44]] The structure of the airways, with the high amount of capillary bed of the alveoli, permits air to come in seal contact with the blood. This makes drug insertion in the airways, in the system of inhalation or aerosol, a helpful route. [[45]] There are three main devices for administering medications by inhalation: 1) Inhalers in pressurized containers, which deliver static volumes by the actuation of a value. 2) Nebulizers, capable of changing aqueous suspensions or solutions (of micronized drug) into an aerosol, either by a high-speed air stream or by ultrasonic energy. 3) Dry powder inhalers, both in single and multi-dose containers. [[46], [38]]

Advantages: [[45], [46], [47]]

1) Direct delivery of the medication be the affected space in the desired form is possible.
2) Dose can be removed without the hazard of contaminating the remaining material in the container.
3) There is larger safeguard against drug degradation by oxygen and moisture, therefore stability is improved for labile substances.
4) As compared to topical implementation, irritation created by mechanical application is reduced or eradicate.
5) It is effortless and suitable to apply the formulation.

Disadvantages: [[45], [46]]

1) There could be drug impatience and toxicity.
2) Drug maintenance and drug clearance can be a problematic.
3) The passage of drug to the site of action is not surefire.
4) Targeting specificity is problematic.

Examples of inhalation drugs: 1) Beta-adrenergic agents (like salbutamol, terbutaline, albuterol), anticholinergic (like ipratropium bromide) & steroids and other anti-inflammatory agents (like beclomethasone, dexamethasone, cromolyn), for asthma. 2) Anticholinergics, Beta-adrenergic agents, Corticosteroids, Cystein derivatives (like acetylevestein), for COPD. 3) Antianginal agents (like nitroglycerin) and Antihypertensives (like nifedipine), as cardiovascular agents. 4) Antidiabetics (like insulin) and Hyperglycemic agents (like glucagon), as blood glucose modifiers. [[48]]

Local/Topical Route: A topical medication is put into a specific part in or on the body. Utmost frequently topical administration suggests that applying to body surfaces like the mucous membranes or skin to treat diseases through a large range of classes containing creams, foams, gel, lotions and ointments. It also refers to the implementation of medication to the surface of the skin or mucous membrane of the eye, ear, nose, mouth, vagina, etc. with the purpose of containing the therapeutic effect of the drug only to the surface or within the layers of the skin or mucous membrane. [[29], [49], [50]]

Mucosal membranes: (antiseptic, eye drops, callous removal, sunscreen, nasal, etc.)
Skin:
Dermal- Rubbing of ointment /oil (for local action).
Transdermal-absorption of drug throughout skin (systemic action).
Stable blood levels.
No first pass metabolism.

Advantages: [[51], [52]]

1) Patient compliance and acceptance.
2) Painless and non-invasive technique.
3) Improvement in drug bioavailability.
4) Beneficial for local delivery of mediators, mainly those which have toxic effects if introduced systemically.
5) Avoidance of fist pass metabolism and the gastro-intestinal incompatibility.
6) Easy elimination of medications when required.
7) Drug delivery selectively to a specific site.
8) Well physiological and pharmacological response.

Disadvantages: [[53]]

1) Chance of local skin irritation at the place of application.
2) Most drugs have a high molecular mass and are poorly lipid-soluble, hence are not absorbed via mucous membrane / skin.
3) Decreased penetration in the affected area.
4) Can be used only for those drugs which need low plasma concentration for action.
5) Enzymes within the epidermis may contaminate the drugs.

Examples of topical preparations intended for systemic or local effect are categorized as: [[54]]

Solids: Dusting powder
Semi-Solids: Creams, Gel, Ointments, Paste, etc.
Liquids: Solution, Emulsion, Liniments, Lotion, etc.

Onset of action: It is the time taken by the drug to produce its action. It is mainly depend on route of administration, for example, oral route will have slow onset of action as compare to intravenous route. This time differs for different types of administration. [[55]]

Table No 5: Onset of action of different route

Route of administration	Time until effect
Intravenous	30 to 60 seconds
Intraosseous	30 to 60 seconds
Endotracheal	2 to 3 minutes
Inhalation	2 to 3 minutes
Sublingual	3 to 5 minutes
Intramuscular	10 to 20 minutes
Subcutaneous	15 to 30 minutes
Rectal	5 to 10 minutes
Ingestion	30 to 90 minutes
Transdermal	Variable (minutes - hours)
Topical	Variable (minutes - hours)

Table No 6: Comparison of the Intramuscular, Intravenous and Subcutaneous Routes: ([10], [28], [29], [56])

Features	**Intramuscular Route**	**Intravenous Route**	**Subcutaneous Route**
Site of administration	Large muscles include deltoid, triceps.	In the vein lumen.	Loose subcutaneous tissue below the skin.
Depot Preparations	Can be made	Cannot be made	Can be made
Absorption speed of Drugs	In between intravenous and subcutaneous	Highest	Slowest
Drug Volume that can be administered	Small volume	Large volume	Small volume
Bioavailability (100%)	75to ≤ 100	100	75 to ≤ 100
Onset of action (Time until effect)	10-20 minutes	30-60 seconds	15-30 minutes
Assistance	Required	Required	Not Required
Irritant Drugs	Soft irritation causing drugs can be given	Can be given	Can't be given
Risk Frequency	Lower than i.v. route	High	Low

Recent Advances in Parenteral Drug Delivery:

There are various drug delivery methods that have been developed as more recent technologies for parenteral drug delivery. These systems contain microspheres, liposomes, niosomes, solid-lipid nanoparticles (SLN's) and pharmacosomes besides others. [[57]]

1. Microspheres: Microspheres are microparticles containing of a solid lipophilic fat core enclosed by a monolayer of phospholipids. [[58]] Earlier, only a peptide suspension / solution were injected intravenously, intramuscularly or subcutaneously. But, the rate of administration was high; this approach required surgical implants which produced discomfort and variations in plasma level of the drug occurred. Therefore, to develop a controlled release parenteral dosage form, peptides were entrapped in implants and used. A newer alternative that emerged was polymers that were liquefied in a biocompatible organic solvent with the drug dispersed in the polymeric solution. [[59]] Both biodegradable and non-biodegradable were been examined and the outcome displays that in case of parenteral delivery, non-biodegradable polymers as carriers remaining within the body after drug release pose toxicity threats. Biodegradable polymers don't show this threat. The major benefit of microspheres is that they can be introduced into the body with a hypodermic needle but this also becomes a drawback as once inserted, they cannot be totally removed from the body in case of an adverse reaction. Parenteral introduction of microspheres needs sterility and their incorporation into a suitable vehicle for injection. It leads to whole absorption of the medication. [[60]] It is also favored over the nasal, vaginal, oral and topical routes as they have an inherent physical and chemical instability and biological short half-lives. [[59]]

2. Liposomes: Liposomes are microscopic structures that comprise an aqueous volume which is encircled by a lipid membrane. [[61]] They mostly comprise one or more lipid bilayers which are concentric and separated by aqueous compartments. [[58]] The drug is existing either in the lipid bilayers or in the aqueous compartment. This drug location depends upon the physical and chemical properties of the drug and the characteristics of the lipids. The important constituents of the liposomes are phospholipids and cholesterol. Liposomes carry out similar functions as compared to controlled drug delivery systems but the release of drug is much quicker. Another difference is that they can alter the distribution pattern of the drug within the body. There may be interaction of the liposome with the cells of the body results to a stage where drug release doesn't happen and the drug and the carrier are taken up by the cells. A main drawback related with liposomal drug delivery is stability. Liposomes are susceptible to both physical and chemical degradation. However, factors like cell liposome interface, a localized drug effect, enhanced uptake of drug and structural flexibility impart liposomes desired characteristics of a suitable drug delivery system. They are utilized in drug delivery of chemotherapeutic medications and vaccines. [[61]]

3. Niosomes: Niosomes are non-ionic surfactant vesicles which can entrap both lipophilic and hydrophilic drugs due to the presence of an aqueous layer and lipid membrane. Nonionic surfactants like Tweens and Spans are used with cholesterol to entrap the drug. They are superior than liposomes in relations of stability and a well discharge and targeting of medications to tumor, brain and liver is reached because of the non-ionic surfactant. Aside from liposomes, this additionally creates them greater to microspheres and nanoparticles. They further suggest the advantages that they not require special conditions for their storage and handling, they attain better bioavailability with minor side effects, they are non-toxic and decomposable and they achieve a greater therapeutic index of the medication by limiting its discharge to the targeted body part only. The main disadvantage is chemical instability because the phospholipids undergo oxidative degradation. Similarly, they may interact

with serum constituents leading to elimination of the lipid layer and leakage of the entrapped drug. They similarly tend to fuse with each other on long time standing leading to a difficulty in their manufacturing process. They have been used as drug carriers for anti-cancer, anti-infective and anti- AIDS medications. Anti-cancer targeting is especially of importance as niosomes can be transported easily to macrophages which infiltrate the tumor cells. These triggered macrophage systems be able to use to transport anti-cancer agents more quantitatively to the tumors. [[62]]

4. Solid-Lipid Nanoparticles: Solid-liquid nanoparticles are a new class of colloidal drug delivery system for intravenous administration. They comprise solid lipid nanoparticles distributed in an aqueous surfactant. Their structure contain of a solid lipid core during which the drug is dissolved enclosed by hydrophobic chains of phospholipids arranged in a monolayer. They will be used successfully for administration of poorly water-soluble medicines. They have the benefit that they show no residues from organic solvent and systemic toxicity and low cardio and they are biocompatible. They are appropriate applicant for sustained drug delivery as multiple, warm microemulsions can be ready. They merge the benefits of fat emulsions, polymeric nanoparticles and liposomes and avoid their drawbacks. Their main benefit over other vesicular systems is that they don't manifest the difficulties of aggregation and drug leakage. Little price of materials, preparation is ease and high entrapment are other advantages. [[63]]

5. Pharmacosomes: They are additionally colloidal dispersions of medicines which can be bound to lipids in a covalent manner. They may be referred to as, thus as the drug delivery system is designed by linking a drug (pharmakon) to a carrier system (soma). They may be available in the form of ultrafine vesicular, micellar or hexagonal aggregates. Their main benefit above other vesicular drug delivery taken is that they are pure drug vesicles which are established by ampiphillic drugs. Any drug owning a mobile hydrogen moiety like –COOH or -OH can be esterified to the lipid and its synthesis can be guided in such a way that results in the improvement of an ampiphillic compound. Similar to liposomes and niosomes, pharmacosomes additionally existing an effective system for targeted drug delivery with fewer toxicity and decreased cost due to their higher bioavailability. [[58]]

CONCLUSION: In this review the differences in routes of administration of various medications and the regional differences in routes of use, have implications for the provision of preventive and treatment services. There are the various routes of administration mainly systemic and local route. In systemic route, the enteral route i.e. oral route is utmost common method of administration. Whereas the parenteral route is the route of choice in case of emergencies. Local route is also used, in which the medication is applied to particular part in or on the body. All this route decides the bioavailability and the onset of action of medication. The novel approaches in drug delivery aid to target the drug to the site of action, which reduces the peripheral adverse effects. Such approaches include microspheres, liposomes, niosomes, nanoparticles and pharmacosomes.

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