

Pharmaceutical Excipients in The Paediatric Formulation

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Abstract

This review focus on the role of excipients used in paediatric dosage of therapeutic agents. This theoretical study seeks to critically review the use of excipients in the paediatric formulation. this review describes the most frequent excipients used in paediatric medicine formulations, identifying the compounds that scientific literature has marked as potentially harmful regarding the side effects generated after exposure. On the other hand, this review also highlights the importance of carrying out safety -checks on the excipients, which, in most cases, are linked to toxicity studies. An excipient in the compilation of paediatric population databases is expected to target safety and toxicity, as in the STEP database. Finally, a promising pharmaceutical form for child population, ODT (Orally Disintegrating Tablets), will be studied. All the excipients and their side effects are covered in this paper. this study of excipients are useful in paediatric formulation study.

Keywords: Surfactant, Galactosemia, Hyperosmolar, Binder, Neonates, Binder

Introduction

The scientific literature suggests that most commercialized drugs are not suitable to be used on the paediatric population, as they are presented in an inappropriate pharmaceutical dosage or form, or because of the excipients they contain. In the face of this reality, compounding is the alternative for paediatric patients. Auxiliary substances or excipients should be used in the development of a compounding formula in order to allow the drug to be administered in an easily and personalized manner. By doing so, the active ingredient will be formulated in a stable, effective, and safe form . The process of formulating excipients in paediatrics is a complicated task that requires various considerations to be accounted for in order to for them to be appropriate; variables such as an acceptable taste, age, dosage forms, among others, must be taken into account when selecting safe excipients. Furthermore, children's rapid growth and development are associated with changes in various organs, body composition, protein bonds, active transport mechanisms and metabolic pathways, which must also be taken into account . In addition to being a complicated task, it is also a critical step in the development of paediatric formulations, as some acceptable excipients in formulations for adult patients are not suitable for paediatric use. It is thus of particular relevance to carry out an assessment of the safety of excipients prior to their use in paediatrics. He specifically recommends that excipient toxicity studies also be carried out, as they provide a detailed assessment of clinical risk. He further suggests that even excipients with significant toxic potential for children may be acceptable after a rigorous assessment of the risk they pose is made. Another factor to be considered for toxicological studies is the extent to which the target disease may be alleviated by the

formulation of that medicine. Thus, pharmaceutical companies should filter the demands for safety assessments by selecting those that will contribute to a potential therapeutic benefit, while helping to develop a reference list of excipients generally considered safe for use in paediatric formulations. In this way, the clinical decision-making process will be made easier. This theoretical study's main objective is to critically review the use of excipients in paediatrics with an emphasis on the issue of safety, mainly on the basis of toxicological studies. This will enable information to be obtained that will allow decisions to be made regarding the masterful preparation of formulations. This study also seeks to investigate the development of databases and initiatives in order to record corroborated information on excipients for paediatric use, thus serving as a guide for clinical professionals.

Ideal properties of good excipient:

1. Excipients range from inert and simple to active and complex substances that can be difficult to characterize.
2. It should be non-toxic.
3. It should not cause any reaction with API's.
4. It should be stable.
5. Excipients should have well solubilizing properties.
6. It should be chemically and pharmaceutically inert.
7. It should be organoleptically acceptable.
8. It should not cause any bioavailability problems
9. It should be compatible with primary packaging materials.
10. It should not have therapeutic activity of its own.

A) Diluents

Lactose, starch and microcrystalline cellulose are often used as diluents, as they are generally safe in the adult population.



1) Lactose:

Lactose, which is a mandatory excipient, is recommended not to be used in patients with lactose intolerance and is contraindicated in patients with galactosemia. It may cause hypersensitivity reactions in children and new-borns. Infants with lactose intolerance do not properly metabolize lactose, due to the deficiency of the enzyme lactase, thus causing the accumulation of lactic acid, hydrogen and carbon dioxide. Symptoms such as severe abdominal pain, flatulence, bloating or swelling and diarrhoea may, therefore, appear, as well as systemic symptoms such as muscle, joint pain and eczema. It should be noted

that children may sometimes have very severe and prolonged reactions to lactose that can lead to additional complications, such as dehydration, bacterial proliferation and metabolic acidosis . Starch, dehydrated calcium hydrogen phosphate, erythritol and cellulose powder are alternatives to lactose in paediatric formulations. They have lactose-like flow properties and produce tablets that can disaggregate in a time less than lactose .

2) Starch

Starch is one of the most commonly used excipients and, in addition to being a diluent, it has binder and disintegrating properties. Due to its properties, starch should be preserved in a dry environment, as it can be an excellent growing medium for microorganisms in case of moisture, which may cause microbiological contaminations. In addition, it may give proliferation of carcinogenic aflatoxins, if contaminated by two species of fungi closely enhanced by each other: *Aspergillus flavus* and *Aspergillus parasiticus* .

3) Microcrystalline Cellulose

Microcrystalline cellulose is a partially depolymerized purified cellulose that is presented as a white, odourless and tasteless crystalline powder composed of porous particles. It is commercially available in different particle sizes and moisture grades that have different properties and applications. It is considered a relatively non-toxic and non-irritating material. It is not absorbed systemically after oral administration and therefore has little toxic potential.

Microcrystalline cellulose is used in pharmaceutical products, mainly as a binder and thinner in tablet and oral capsule formulations. In addition to its use as a binder and thinner, it also has some lubricating and disintegrating properties that make it useful for forming tablets .

B) Solvents

Some of the most common solvents are water, ethyl alcohol, propylene glycol (PG), glycerol and polyethylene glycol.



1) Water

Water is the most commonly used agent in paediatric formulations, as liquid preparations are easier to administrate and allow a more accurate dose adjustment . Water is an ideal medium for the proliferation of microorganisms (bacteria and fungi) despite their purification, which is why antimicrobial agents have

to be added. In paediatric oral formulations, the total volume of fluid is of vital importance for the taste and ability to adequately measure the volume to be administered: in children under 5 years of age a volume of less than 5 mL should be administered and, in children under 10 years of age, a volume of less than 10 mL should be administered.

2) Ethyl Alcohol

(Ethanol) Ethanol is one of the excipients of concern to international health regulatory agencies, as it causes neurotoxicity and cardiovascular problems in the paediatric population; it is a potentially harmful excipient in neonates. For this reason, permissible maximum limits have been set and, in some countries, non-alcoholic medicines are to be established. It is a very permeable excipient with regard to the blood–brain barrier, and the one most commonly used in oral medicinal products, reaching 63% of cases . It is rapidly absorbed into the gastrointestinal tract and is primarily metabolized in the liver to acetaldehyde, which is oxidized to acetate.

Indeed, Macrel and Bernardo’s review of liquid formulations in Brazil has furthered our understanding of the high use of ethanol. These researchers demonstrated that ethanol is used in various concentrations and functions: as solvent (main function), cosaver, flavouring agent, preservative and as an extraction solvent in herbal medicines . It also has antimicrobial properties and increases the permeability of many preparations .

The use of ethanol as an excipient carries potential hazards and adverse effects, which are already observed at a dose of 100 mg/dL. These effects include hypoglycaemia, acidosis and hydro-electrolytic alterations. Very high intake can lead to stupor, coma, respiratory depression and cardiovascular collapse. Hypoglycaemic seizures may also occur in children . For all these side effects, any alcohol should be avoided in paediatric forms. However, it is still used in many liquid preparations, because it is the only solvent that allows the solubilization of certain active substances .

In both the United States and the European Union, guidance on maximum ethanol limits in medicinal formulations is increasing . According to the World Health Organization and a regulation existing in the United States, the maximum alcohol content in paediatric formulations should not exceed the limits specified in Table A1.

It should be noted that ethanol was also able to interact with many active substances of other medicines that the child is taking and, therefore, possible interactions must be studied prior to concomitant administration. Furthermore, new contributions in the scientific literature on excipients, including ethanol, is expected to help health professionals predict the risks of using a particular excipient, especially in the paediatric population. For example, the guideline excipients in the label and package leaflet of medicinal products for human use alerts on the risk of the use of ethanol and proposes changes on its use.

3) Propylene Glycol (PG)

PG is used as a solvent to stabilize substances that are not water soluble, in parenteral and non-parenteral formulations. It also has moisturizing, antimicrobial properties and can be used as plasticizer. It is rapidly absorbed through the gastrointestinal tract and damaged skin and metabolized in the liver to lactic acid and pyruvic acid . Exposure to high doses of PG may affect the Central Nervous System, especially in new-borns and children under 4 years of age .

Due to children’s physiological and metabolic immaturity, PG can accumulate rapidly causing toxicity . In new-borns, its half-life is very long, almost seventeen hours, compared to that of adults, which is about

five hours . The GRAS (Generally Recognized as Safe) classification of excipients typically does not consider the differences in physiological and metabolic maturation between the paediatric and adult populations , a fact that justifies some important adverse reactions presented by PG in the paediatric population:

- Hyperosmolar syndrome in burnt children with topical arsenic sulfadiazine ointment containing PG.
- Precipitation of irreversible deafness in pretermits who received a multivitamin complex containing PG.
- Parenterally it is possible to observe haemolysis, seizures, respiratory depression, hypertension.
- Contact dermatitis is topically observed.

In the 1980s, cases of biochemical abnormalities, including hyperosmolarity, lactic acidosis and elevated levels of creatinine and bilirubin, were documented after exposure to 3 g/day of PG and for at least 5 consecutive days. Clinical symptoms, including seizures and bradycardia episodes , then appeared. In 2011, the U.S. FDA reported health problems in premature new-borns associated with the use of Kaletra® (lopinavir/ritonavir) solution; liquid preparation containing high amounts of PG and ethanol.

Exposure to PG in new-borns and children under 4 years of age remains common, despite historical and contemporary reports dealing with toxic adverse effects of this excipient. Thus, the study of Allegaert J. in terms of the PG research project in new-borns is of great interest, as it provides scientific evidence on the tolerance and plasma clearance of this excipient, including differences in elimination pathways (renal pathway compared to the hepatic pathway).

4) Glycerol

Glycerol, a mandatory excipient (E-422), is used as solvent, sweetener, viscosizer and preservative. When used at high concentrations (more than 40%), it can cause mucositis in the stomach, as well as diarrhoea and electrolyte disturbances due to its hygroscopic and osmotic properties. Therefore, a maximum amount of 10 g/dose has been established.

In the adult population glycerol has few adverse effects. However, cases of neurological toxicity have been reported in the paediatric population . Polyethylene Glycol (PEG) PEG is a polar and water-soluble substance used as a co-solvent, suspensor and viscosity agent. The PEG 400 is the most used in liquid formulations. It may cause some laxative effect when taken orally, with the maximum daily dose established in adults at 10 mg/kg/day . PEG has low oral bioavailability and renal elimination. Due to its properties, significant adverse effects such as diarrhoea and nephrotoxicity have been reported, so the maximum recommended daily dose is 10 mg/kg body weight . It can also cause some laxative effect when taken orally. When newborns and infants are exposed to high doses of PEG, gastrointestinal disorders, adverse effects typical of alcoholic solvents may occur.

C) Coating Agents



1) Phthalates

Phthalates play a primary role as a coating agent (film-forming, plasticizer) in medicinal formulations. Exposure of pregnant women to phthalates has been associated with abnormalities in the development of the foetus, such as cleft palate and skeletal malformations; abnormalities that can end in stillbirth. It was observed that they have a high potential to produce toxicity in the development of experimental animals, as well as in their reproduction. Due to these risks of certain phthalates to health, in March 2012, the CDER published a guide to orient the pharmaceutical industry on the use of phthalates: —Limiting the use of certain phthalates as excipients in CDER regulated products. This guidance document recommends limiting the use of certain phthalates, such as dibutyl phthalate (DBP) and di(2-ethylhexyl) phthalate (DEHP).

D) Preservatives

Preservatives are a group of excipients that prevent microbial growth and, consequently, the degradation of the active substance and the possible alteration of the organoleptic characteristics of the final formula. The American Academy of Paediatrics does not recommend the use of preservatives in reparations for patients under 3 years of age due to the lack of physiological and metabolic maturation of these patients. This lack of maturation may lead to the accumulation of preservatives in the liver, a fact that increases the risk of cardiovascular collapse, in addition to producing non-specific reactions or even allergies. It should be noted that preservatives are not contraindicated in children under 3 years of age, but should only be used in imperative cases.



1) Sodium Benzoate

Sodium benzoate is a preservative widely used in pharmaceutical and cosmetic formulations, at concentrations between 0.02% and 0.05%. Its maximum activity occurs in weakly acidic pH 4.5 solutions and is inactive at pH values greater than 5.

As side effects, it can cause contact hives and other allergies. In premature children, its use is contraindicated, as it presents a risk of metabolic acidosis and jaundice.

One of the large prospective studies conducted by Nellis and collaborators in hospitalized neonates in Europe described the administration of eight potentially harmful excipients of interest (EOI) (parabens, polysorbate 80, propylene glycol, benzoates, sodium saccharine, sorbitol, ethanol and benzalkonium chloride) and identified risk factors resulting from exposure. Neonates appear to lack the ability to

conjugate benzoates with glycine, leading to the accumulation of benzoic acid that can cause metabolic acidosis and neurotoxicity. The ESNEE (European Study of Neonatal Exposure to Excipients) clinical study showed that sodium benzoate was found in 10 medicines given to new-borns, despite being a highly toxic excipient to them. Preservatives such as parabens (and their sodium salts) and propyl para-hydroxybenzoate were also found in 24 paediatric medications, and ethanol in 8.

2) Benzyl Alcohol

Benzyl alcohol presents antibacterial properties. For that reason, it is used as a preservative in a lot of medicines. Its activity depends on the pH; being at it is maximum at a low pH (between 2.5–4.5). It is used at the concentration of 0.01–0.15% in oral preparations.

In adults, it is metabolized to benzoic acid, which is conjugated in the liver with glycine. As a result, the acid hippuric formed is excreted in urine. However, in new-borns, this conversion of the benzoic acid into hippuric acid is very diminished, because of the lack of liver maturation. That justifies fatal intoxication cases in new-borns who had their umbilical catheters cleaned with benzoic acid. Consequently, cases of metabolic acidosis and respiratory depression occurred. Additionally, other adverse effects have been described, like intraventricular bleeding, cerebral palsy and developmental delay. In some cases, there have been reactions of hypersensitivity, allergy and contact dermatitis.

In the 1990s, Svinning and collaborators conducted a review of the medical records of babies who weighed less than 1250 g at birth and were admitted to the neonatal intensive care unit. The main objective of this study was to assess the impact of the toxicity of benzyl alcohol, following discontinuation of the use of solutions to wash intravascular catheters containing benzyl alcohol. A significant decrease in mortality rate and incidence of Grade III/IV intraventricular haemorrhage was observed among infants weighing less than 1000 g at birth who were not exposed to benzyl alcohol (as opposed to those who were). The maximum dose of benzoic acid (and other benzoates, calculated as benzoic acid) recommended by WHO is 5 mg/kg body weight per day in adults, a dose that, in children, logically, should be much lower. As the effects on new-borns are severely toxic, the U.S. FDA has recommended the exclusion of benzyl alcohol from medications, intravenous fluids, and heparin washing solutions for them. The EMA states that any medicine containing benzyl alcohol —should not be given to premature babies and new-borns. In fact, currently, any exposure to benzyl alcohol is contraindicated in children under 3 years of age.

3) Benzalkonium Chloride

Benzalkonium chloride is a quaternary ammonium used in ophthalmic preparations at a concentration of 0.01–0.02% (v/v). Generally, it is non-irritating or sensitizing and is well tolerated in skin solutions. As a side effect, it can cause bronchoconstriction in asthmatic patients, if used in nebulization solutions. Furthermore, cases of ototoxicity may occur in otic preparations, hypersensitivity in topical skin preparations and respiratory failure in infants who ingest this excipient, with this side effect being the most severe.

4) Thiomersal

Thiomersal is a preservative widely used in vaccines and topical preparations, such as eye drops. Its toxicity is similar to mercury: in fact, it contains a mercury atom in its molecular structure. The concentration used depends on the medicinal product: in injectable preparations 0.01% is used and in

ophthalmic solutions between 0.001% and 0.15% . Several allergic hypersensitivity reactions (e.g., erythema, vesicles) have been reported. Therefore, health authorities have recommended their withdrawal from vaccines at risk of toxicity. Recently, thiomersal has also been implicated in the onset of autism spectrum disorders in children who received aluminium salt vaccines as an adjuvant. Accordingly, various countries (including Spain) no longer market paediatric vaccines with this component . The use of single-dose vials is recommended in many cases to prevent the use of preservatives such as thiomersal or sulphites such as sodium metabisulphite .

5) Parabens

Parabens are the most commonly used preservatives (also in cosmetics and foods), due to their wide antimicrobial spectrum and their effectiveness over a very wide pH range (between 4 and 8).

Parabens are of mandatory declaration. They are used at concentrations between 0.01 and 0.2% , although it is most common to use a mixture in proportion 10:1 (0.2% methylparaben + 0.02% propylparaben). The maximum recommended daily dose is 10 mg/kg body weight.

They may produce a cross-hypersensitivity reaction in patients allergic to aspirin. This is because the main metabolite of parabens is hydroxyparabenzoic acid, structurally very similar to aspirin . Recent pharmacovigilance studies have highlighted certain questions about the purported safety (non-teratogenic or carcinogenic) of parabens.

Alternatives should therefore be found, especially in paediatric formulations. Antimicrobials are not necessary for parenteral formulations. The absence of parabens and benzoates in 85% of parenteral prescriptions suggests that administration of these excipients can be largely avoided.

E) Antioxidants

An antioxidant is a molecule that inhibits the oxidation of other molecules. Oxidation is a chemical reaction that transfers electrons or hydrogen from a substance to an oxidizing agent.



➤ Ideal Properties of Antioxidants:

- 1) Effective at a low, nontoxic concentration
- 2) Stable and effective under normal conditions of use, over a wide pH and temperature range
- 3) Soluble at the required concentration
- 4) Compatible with a wide variety of drugs and pharmaceutical excipients
- 5) Free from objectionable odor, objectionable taste
- 6) Colorless in both the original and oxidized form
- 7) Nontoxic both internally and externally at the required concentration

- 8) Reasonable cost
- 9) Unreactive (does not adsorb, penetrate, or interact) with containers or closures

1) Sulphites

Sulphites are antioxidants widely used in different formulations; sodium sulphite, sodium bisulfite, sodium metabisulphite and potassium metasulfide are the most common.

Regulatory agencies (e.g., FDA, EMA) consider excipient sulphites safe. However, they present risks and possible fatal side effects derived of their use. One of the most common cases occurs in asthmatic patients, who may develop severe bronchospasm if they take medicines containing sulphites in their formulation.

The antioxidants constitute a group of compound chemists used to avoid the oxidation of the active principles in the formulations .

It should be noted that a large number of people are sensitive to sulphites and may experience a variety of symptoms, including dermatological, gastrointestinal and respiratory symptoms. However, reactions that develop in the respiratory tract explain most cases of sensitivity to sulphites. It is important to note that several individuals experience a variety of symptoms after exposure to sulphites; therefore, skin, intestinal and respiratory reactions can occur simultaneously and in various combinations and severity. People with sensitive skin who regularly use cosmetics or topical medications containing sulphites have chronic skin symptoms, especially on the hands, perineum and face. Sensitivity to sulphites is a very real problem that significantly affects the health of many people, especially asthmatics. Sensitivity to sulphites should be considered when people show adverse reactions to a variety of exposures, without an obvious pattern, particularly when those people experience worsening asthma symptoms after consumption of foods such as dried fruits and wines, or adverse skin reactions, after the use of cosmetics or medicinal creams.

2) Propyl Gallate

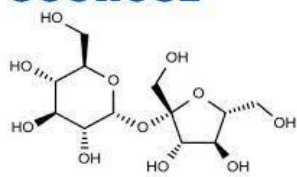
Propyl gallate is an antioxidant used to prevent the breakdown of fatty acids. It is used at a concentration of 0.1% and also has a synergistic effect with other antioxidants. In neonates it can cause dermatitis, skin allergy and methemoglobinemia.

F) Sweeteners

The use of sweeteners varies between routes of administration and, like preservatives, are not necessary in parenteral administrations . They have been linked to photosensitivity reactions, diarrhoea and poor absorption of nutrients. The most commonly used sweeteners in pharmaceutical formulations are sucrose, sorbitol, mannitol, aspartame and sucralose.

1) Sucrose

SUCROSE



O- α -D-glucopyranosyl-(1 \rightarrow 2)- β -D-fructofuranoside

Sucrose is a natural disaccharide that is hydrolysed in the gut into two monosaccharides: glucose and fructose. In children with type I diabetes, the use of sucrose should be avoided. Very high concentrations (up to 35% are used for liquid formulations such as syrups). When the patient needs prolonged treatment with these preparations, he or she is at risk of dental damage. It has also been described that administration at very high doses on a daily basis may be carcinogenic.

2) Sorbitol

Sorbitol is a monosaccharide that is not absorbed into the digestive tract and is therefore considered safe in paediatric patients, although it is laxative at high doses. It is also used as a diluent as well as capsule plasticizer. Sorbitol is another example of an excipient that causes gastrointestinal disorders, such as abdominal pain, swelling, flatulence, vomiting and osmotic diarrhoea. Because sorbitol is metabolized to fructose, it should be avoided on children with fructose intolerance and hypoglycaemia. In isolated cases it can cause liver damage leading to coma and even death. In infants the accumulation of sorbitol can lead to diabetic complications such as retinopathy and cataracts. Therefore, the amount of sorbitol is limited to 0.3 mg/kg in paediatric formulations.

3) Mannitol

Mannitol is used as a sweetener and as a diluent. It has been linked to severe anaphylactic reactions in paediatrics. As in the case of sorbitol, it is not absorbed into the digestive tract, so it has laxative properties at high doses.

4) Aspartame

Aspartame is an artificial sweetener that has 180 and 200 times more sweetener power than sucrose. Because of this, it is the most used sweetener in the pharmaceutical and food industry. It is a disaccharide made of an aspartic acid and a methyl phenylalanine ester. It is an excipient of mandatory declaration and its maximum dose has been set at 40 mg/kg body weight. Phenylalanine is very harmful for patients with phenylketonuria, as well as for pregnant mothers who carry a foetus of such metabolopathy. The use of aspartame in patients with phenylketonuria should be avoided. The adverse effects of aspartame that have been described are: neurological (neurotoxicity, epilepsy, headache, panic attack and hallucinations), hypersensitivity reactions (vascular and granulomatous panniculitis) and cross-reaction with sulphonamides.

5) Saccharine

Saccharine is also an artificial sweetener 300–600 times stronger than sucrose, but if not used properly it can leave a residual bitter taste. Your daily dose should not exceed 2.5 mg/kg body weight. It is recommended to limit the daily dose in children and pregnant women. Currently, controversy about its safety remains present, as in adults it has been linked to bladder cancer when used at very high doses. Adverse effects of saccharine include hives, itching, photosensibilization, eczema, as well as nausea and diarrhoea.

6) Sucralose

Sucralose has a sweetener power between 100 and 300 times higher than sucrose. Its maximum daily dose is 15 mg/kg in weight. Sucralose is a non-toxic compound and is also not irritating, but it is not considered

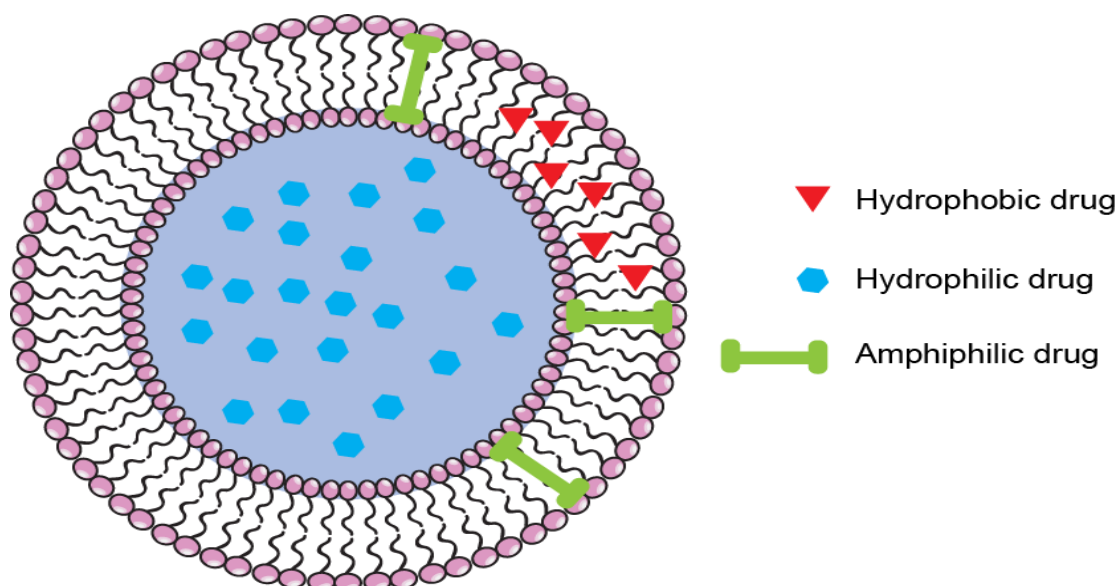
totally inert. It can increase the expression of cell flow transport protein glycoprotein P and two cytochrome P450 isoforms, which are essential substances in the drug purification process. Furthermore, sucralose alters the composition of the microbiome of the digestive tract, which ends up causing the reduction of the proportion of beneficial bacteria. In addition, if cooked at high temperatures, chloropropanol can form, which is a toxic compound. It can also alter the patient's levels of glucose, insulin and glucagon-like peptide type 1 (GLP-1).

G) Surfactants

Properties of surfactants:

A surfactant must fulfill two structural requirements:

- a) A surfactant must contain a lipophilic region.
- b) A surfactant must contain a hydrophilic region.



In a surfactant both hydrophilic and lipophilic region must be balanced because then both the regions will be concentrated at an interface and therefore surface tension will be lowered

1) Polysorbates:-

Polysorbates are partial esters of sorbitol fatty acids and their copolymerized anhydrous with ethylene oxide. They are used as dispersant agents, emulgents, non-ionic sanitary surfactants, solubilizers, and moisturizers, among other things. In general, they are considered non-toxic and non-irritating. However, they have been associated with serious side effects, including deaths in under-weight neonates who received vitaminE preparations with this substance. In addition, polysorbate 80 has been associated with increased mortality in new-borns.

H) Colorants

Colorants are excipients used to facilitate the identification of the formula by parents and patients. The most commonly used dyes are whip dyes, quinolones, triphenylmethane and xanthine's.



Tartrazine (yellow number 5) has been implicated in anaphylactic reactions, edema, asthma, bronchospasm, eosinophils, angioedema and hives in patients with sensitivity to it. It appears to cause histamine degranulation of mast cells. As a result, most global regulatory agencies restrict the use of dyes such as tartrazine, because azo dyes have been linked to hypersensitivity and ADHD reactions in children. These dyes can be replaced by plant dyes such as annatto, malt beta-carotene and turmeric and should not be used at all in paediatric formulations.

Conclusion:

Excipients can play an important role in formulating various dosage forms. Excipients have been used as a main secondary tool in formulations. They are also increasingly used as taste-masking, stabilizing, and protective agents in oral drug delivery. Some excipients can bind the particles of a solid dosage form and also change the flow properties of a liquid dosage form. Extensive applications of excipients in drug designing have been realized because excipients offer unique properties which so far have not been attained by any other materials. Understanding the basic concepts of excipients provides a foundation for further understanding of drug products and designing of better delivery systems. This review can serve as a valuable source of information for those with little or no background in excipients, researchers in the pharmaceuticals and biomedical areas, as well as pharmacy students. Various information and properties of excipients studied in this review.

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