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# CLASSIFICATION AND PROPERTIES OF SELCTED EXCIPIENTS AND ACTIVE PHARMACEUTICAL INGREDIENTS

**Anil Kumar Patel**
Research Scholar, Sunrise University,Alwar, Rajasthan

**Dr. Manmeet Singh Saluja**
Research Supervisor, Sunrise University, Alwar, Rajasthan

## ABSTRACT

Pharmaceutical raw materials include both active pharmaceutical ingredients (APIs) and inactive substances (excipients). Excipients are inert components used to carry the API, whereas pharmaceutical active ingredients (APIs) are the active chemicals in a medication that cause the drug to have the desired pharmacological effect. Concerns about the safety of the excipients, food components, and active pharmaceutical ingredients (APIs) used in paediatric formulations have prompted increased scrutiny from regulatory agencies throughout the world in recent years. Despite the Federal Food, Drug, and Cosmetic Act of 1938 requires such testing prior to inclusion into formulations, surprisingly few excipients have been subjected to a randomised controlled trial in a juvenile subpopulation.

**KEYWORDS:** - Food products, population, co-processed excipients, randomized clinical trial.pharmaceutical ingredients

## INTRODUCTION

Because of these concerns, regulatory agencies throughout the world have focused particularly on the excipients, food additives, and APIs used in paediatric formulations. Because of their pharmacological action, several excipients have been associated to possible delays in childhood development. Few excipients have passed randomised clinical trial (RCT) in paediatric subpopulation, despite the fact that the Federal Food, Medicinal, and Cosmetic Act of 1938 requires thorough safety testing of raw chemicals used in medicinal products before they may be incorporated into formulations. Because of changes in their absorption, distribution, metabolism, and excretion (ADME) profile, for instance, newborns and infants may be more sensitive to an excipient than a toddler. This means that few excipients are considered "safe for eating" by kids. In this chapter, we'll take a look at several common excipients and active pharmaceutical ingredients (APIs) used in children's medicines, focusing on their chemical make-up, how they react with other substances, and the safest possible daily amount for use.

The global APIs (Active Pharmaceutical Ingredients) market is expected to reach $198.8 billion by 2022, a CAGR of 6.4% from 2017 to 2022. The government's initiatives, regional penetration,

an ageing population, and the expiration of patents on popular drugs are all factors driving the business ahead. The API sector is hampered by the World Health Organization's (WHO) strict validation and safety requirements and a fragmented market. The generic/non-branded segment of the industry saw the largest market share throughout the forecast period because to rising healthcare expenditures, government attention on generics for cutting healthcare costs, and contracting pipelines of global pharmaceutical products. Over the forecast period, Asia Pacific is expected to have the greatest market share due to favourable factors including low operational costs and major investments in medical research. Due to the high cost of trained labour and energy, the European market was also forced to move its headquarters to growing nations like India.

Excipients are additions used in pharmaceutical formulations for purposes such as increasing volume, enhancing medication absorption, boosting stability, and preventing denaturation. Excipients used in pharmaceuticals are safe, affordable, stable, and easy to work with. Various pharmacological forms, such as capsules, tablets, oral liquids, inhalers, implants, and injections, may contain excipients. According to ASD Reports, the increased demand for oral pharmaceuticals is fueling growth in the pharmaceutical excipients market throughout the world. Increasing demands are being placed on the pharmaceutical industry to supply oral solid dosage medications with specific benefits, such as higher patient compliance and simple dosing. Functional excipients have proved incredibly helpful in the development of treatments for APIs with limited solubility, as well as in the development of delayed release dose formulations of existing drugs, which can increase the product's shelf life and revenue. The Latin word excipere, from which we get the word "excipient," implies "to except" or "other than." Pharmaceutical excipients refer to all of the inactive constituents of a medication. Excipients are supposed to be safe, however reports of adverse effects suggest otherwise.

## LITERATURE REVIEW

**Shilpa P Chaudhari (2012)**Excipients play a significant role in the development of dosage formulations. They are a part of the dosage forms alongside the pharmacological active ingredients. In addition to serving as protective agents, bulking agents, and in some cases increasing bioavailability of pharmaceuticals, excipients come in a wide variety of forms and come from a variety of sources, as will be discussed in this review. Some excipients are more suited to a given dosage form than others, and this review investigates the selection criteria for excipients and the multiple interactions an excipient could face over the length of its stay in formulation to explain why. Preventing excipient interactions that might be damaging to the medicine is essential. You may read more about this under the interactions subsection. Just like any other active pharmaceutical component, excipients require a standardisation and stabilisation process, as well as safety evaluation standards, which are outlined in the following review.

**RounakChourasia et.al. (2022)**The essay set out to provide a bio-based economic framework predicated on the effective utilisation of agricultural biomass in the production of innovative bio-based goods (such as medicines and active pharmaceutical components). We also look at more theoretical approaches to bioenergy, in addition to our main focus on the production of bio-based commodities and biofuels. This review article elaborated on the fundamental ideas behind producing these by-products. In order for small-scale farmers to successfully fulfil regional demands for bio-based materials and energy, it is crucial to advance the development of such

products. While smaller markets expand, they create the infrastructure that allows for the growth of bigger ones. The primary objective of this study is to investigate how biotechnological innovations may bring together underprivileged farmers and underdeveloped areas, therefore reducing the burden on biomass production infrastructure.

**Liyu Liu, et.al. (2022)**Cocrystallization has emerged as one of the most successful approaches in the last several decades for addressing API stability difficulties. However, structural analysis and understanding of the complexity of the degradation process have prevented extensive investigation into the molecular basis of the enhanced stability. The purpose of this work is to demonstrate that stable cocrystals are not accidental but rather the result of deliberate design, exact adjustment, and creative construction. A recommendation of an individual cocrystal strategy is not only possible, but also crucial, in mitigating environmental impacts (heat, moisture, light, and oxygen). More stability may be produced by modifying the contact strength, molecular shape, packing patterns, and electronic effect, as described below. Individual examples of notable cocrystals that have overcome comparable stability issues are provided, explaining the critical structural features in different contexts and providing new opportunities for developing stable cocrystals in the future.

**Goyal, Prateek et.al. (2022)**To ensure a drug's long-term stability, it must be formulated with a number of different substances, some of which are called excipients. Excipients are substances added to a formulation that don't contribute to its primary effect. They are essential in the production and distribution of safe medications. The ideal excipient would not provide any visible therapeutic benefits, yet would nonetheless improve the drug's bioavailability. Throughout the medication development process, it is vital to select the suitable excipients (or mix of excipients) for the intended therapy.

**Saito, J.; (2022)**It is difficult to produce paediatric formulations because of the lack of information on the safety and toxicity of certain commonly used excipients. Although the maximum safe oral dose for many excipients in adults is established, this is not the case for paediatric patients or preterm newborns due to a lack of data. There are four parts to this research. This review will concentrate on four key areas with the goal of ensuring the safe use of excipients: (1) the current situation, (2) comparing and contrasting country-specific viewpoints, (3) historical and ongoing collaborative efforts, and (4) future perspectives on excipients for paediatric formulation. Because of this work, a regulatory framework for pharmaceutical excipients is already in place. Poor regulation and a lack of data were found in certain areas, although there are gaps in coverage in other regions. Despite continued efforts to raise issues on excipient exposure, build a region-specific database, and strengthen excipient regulation, there is a lack of evidence-based information on the safety of children's products. Establishing unequivocal safety limits, collecting quantitative data on excipients of concern in the paediatric population, and harmonising regulatory regimes for excipients throughout the world all require further investigation.

**Excipients**

Excipients are "inactive" substances that are generally recognised as safe (GRAS) for human consumption and are licenced for usage in the pharmaceutical business. Excipients are added to active pharmaceutical ingredients (APIs) to improve their stability, accuracy, precision, uniform blending, mask unpleasant taste, improve flowability, add bulk density, and regulate the release of

API. This helps to maximise patient compliance, bioavailability, efficacy, and minimise toxicity. Although excipients are "inactive" and therefore not have to be disclosed on other drug products, they must be listed on ophthalmic, topical, and parenteral pharmaceutical products in accordance with the FDC Act. Therefore, excipients undergo significant short-term and long-term toxicity study prior to inclusion in pharmaceutical goods for the adult population, but are not examined in the paediatric subpopulation. Challenges for research involving children include ethical concerns, a lack of readily available blood samples, and developmental changes that occur between infancy and adulthood. Because of the rapid pace of growth and development in children, data from clinical studies demonstrating efficacy and dosing regimen in an adult population cannot be extrapolated to a paediatric population. Today, children can have their meds via a wide variety of delivery systems, including drops, elixirs, syrups, suspensions, sprinkles, capsules, orally disintegrating pills, chewable tablets, injectables and so on. When used in paediatric formulations, several excipients, including lactose and sorbitol, can induce diarrhoea in young patients. Children who consume sweeteners made with aspartame are at increased risk for developing neurological disorders including seizures and headaches. Therefore, this section will examine the excipients often used in children's medications, the chemical reactivity of the functional groups included within the molecules, the impurities, and the doses at which the excipients exert their toxicity.

**Classification of Excipients**

Excipients can be broken down into several categories based on (1) their origin (plant, animal, mineral, or synthetic), (2) their function in the formulation (binders, diluents, disintegrants, fillers or bulking agents, glidants, lubricants, colouring agents, preservatives, sugars, surfactants, solvents, coating agents, etc.), and (3) the types of chemical substituents they contain (e.g., hydroxyl, sul The excipients used in children's drugs are listed in Table-1.

**Table-1 Classification of pharmaceutical excipients**

1. Classification of pharmaceutical excipients based on function
   - Binders
     - *Example*: PVP, HPMC
   - Coloring agents
     - *Example*: E number colorants
   - Coating agents
     - *Example*: Phthalates
   - Diluents
     - *Example*: Lactose, microcrystalline cellulose
   - Disintegrants
     - *Example*: Sodium starch glycolate, croscarmellose sodium
   - Fillers/bulking agents
     - *Example*: Lactose
   - Glidants
     - *Example*: Colloidal $SiO_2$
   - Lubricants
     - *Example*: Magnesium stearate, sodium stearyl fumarate, sodium behenate
   - Preservatives
     - *Example*: Sodium benzoate, thiomerosal
   - Sweeteners
     - *Example*: Sorbitol, mannitol, dextrose, aspartame, saccharin, sucralose
   - Surfactants
     - *Example*: Tweens, spans, polysorbates, poloxamers, lecithins
   - Solvents
     - *Example*: Ethyl alcohol, benzyl alcohol, propylene glycol, sorbitol, PEGs

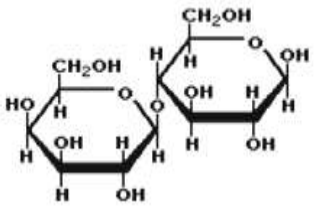
2. Classification of pharmaceutical excipients based on origin of source
   - Animal source
     - *Example*: Lactose, gelatin, stearic acid
   - Mineral origin
     - *Example*: Silica, calcium phosphate
   - Plant source
     - *Example*: Alginates, starches, sugars, cellulose
   - Synthetic excipients
     - *Example*: Polyethylene glycol, polysorbates, polyvinylpyrrolidone
3. Classification of pharmaceutical excipients based on chemical substituents
   - Alcohols
     - *Example*: Ethyl alcohol, benzyl alcohol, propylene glycol
   - Carboxylic acids
     - *Example*: Benzoic acid
   - Carbohydrates
     - *Example*: Mono-, di- and polysaccharides, sucrose, lactose, mannitol
   - Dyes
     - *Example*: Tartrazine, amaranth
   - Esters/ethers
     - *Example*: Fatty acid esters or ethers
   - Glycerides and waxes
     - *Example*: Peanut oil, bees wax
   - Halogenated hydrocarbon derivatives
     - *Example*: Freons, chlorbutol, halothane
   - Organic mercurial salts
     - *Example*: Thiomerosal
   - Phenolic compounds
     - *Example*: BHA, BHT
   - Proteins
     - *Example*: Albumin, gelatin
   - Polymers
     - *Example*: HPMC, Eudragits

**Properties of Selected Excipients**

At high enough doses, any excipient might be dangerous to kids. According to the 2005 FDA Guidance document, excipients for paediatric formulations should be chosen based on the ADME profile of the target patient population, the treatment duration, and the dosing interval. Additionally, commonly used excipients, such as the quantity or absence of preservatives like thimerosal, benzyl alcohol, and propylene glycol, may be altered in vaccines and other medicine products administered to children less than 6 years old. Substitutes for the preservatives thimerosal, benzyl alcohol, and propylene glycol in vaccines and other pharmaceutical preparations include methyl and propylparaben (0.1-0.3%), benzalkonium chloride, bronopol (2-bromo-2-nitropropane-1,3-diol), sodium azide, and 2-phenoxyethanol.

**Fillers/Binders**

Lactose



Synonyms: Lactin; Lactose; D-Lactose; Galactinum; Aletobiose; Osmolactan; Lactobiose; Milk sugar

General appearance: White powder, either in crystalline or amorphous state

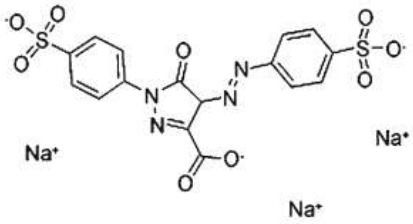
Molecular formula: $C_{12}H_{22}O_{11}$

Formula weight: 342.3 g/mole

Water solubility: Very soluble in water (5–10 g/100 mL)

Coloring Agents

Tartrazine



Synonyms: CI NO 19140; CI acid yellow 23; CI 19140; E102; Lake tartrazine; Kiton Yellow T; Hydrazine yellow; Food yellow No. 4

General appearance: Deep yellow powder

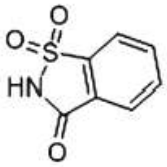
Molecular formula: $C_{16}H_9N_4Na_3O_9S_2$

Molecular weight: 534.36 g/mole

Water solubility: Very soluble

**Sweeteners**

Saccharin



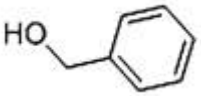
Synonyms: Saccharin; Saccharin 550X; Syncal ®, o -benzoic acid sulfimide

General appearance: White crystals, odorless or faintly aromatic odor, sweet in taste.

Molecular formula: $C_7 H_5 NO_3 S$ Molecular weight: 183.18 g/mole

**Alcohols**

Benzyl Alcohol



Synonyms: (Hydroxymethyl) benzene; Bentalol; Benzalalcohol; Benzalcohol; Benzenemethanol;

General appearance: A clear colorless liquid with a pleasant odor, slightly denser than water, flash point 194 °F, boiling point 401 °F, contact may irritate skin, eyes, and mucous membranes.

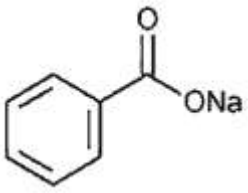
Molecular formula: $C_7H_8O$

Molecular weight: 108.14 g/mole

Water solubility: Very soluble

**Preservatives**

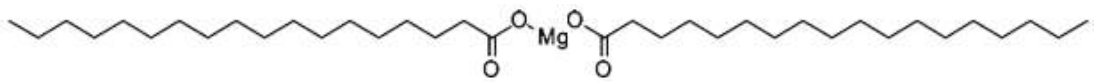
Sodium Benzoate



Synonyms: Benzotron(r); benzoic acid sodium salt; Fema 3025
Molecular formula: C 7 H 5 NaO 2
Molecular weight: 144.1 g/mole
Water solubility: Soluble

**Lubricants**

**Magnesium Stearate**




Synonyms: dibasic magnesium stearate; Dolomol; magnesium di-stearate; Magnesium stearate medicinal; stearate de magnesium: magnesium octadecanoate

General appearance: White powder

Molecular formula: $C_{36}H_{70}MgO_4$

Molecular weight: 591.24 g/mole

Water solubility: Insoluble

## CONCLUSION

The availability of paediatric patients, blood samples, and the difficulty of extending findings to the paediatric subpopulation all pose challenges for RCTs assessing the safety of excipients. Since it is very unlikely that all excipients would be exposed to RCT in paediatric population such that the recommended daily intake could be determined, it is also unlikely that there would be a list of "chosen excipients" that may be used specifically in paediatric populations. For this reason, it would be useful for researchers to evaluate the excipients' safety profiles in children as part of drug discovery. Neither would there be a list of "selected excipients" that can be used solely in paediatric population because it is extremely doubtful that all excipients would be exposed to RCT in paediatric population such that the recommended daily intake could be determined. Therefore, it would serve the scientific community well to assess the excipients' safety profile in the paediatric population as part of the therapeutic development process.

## REFERENCES

1. Shilpa P Chaudhari (2012) Pharmaceutical Excipients: A review IJAPBC – Vol. 1(1), Jan- Mar, 2012

2. RounakChourasia, SrichandanPadhi, LoreniChiringPhukon, MdMinhajulAbedin, RanjanaSirohi, Sudhir P Singh, Amit Kumar Rai. (2022) Peptide candidates for the development of therapeutics and vaccines against β-coronavirus infection. Bioengineered 13:4, pages 9435-9454.

3. Liyu Liu,2022 Enhancing the stability of active pharmaceutical ingredients by the cocrystal strategyIssue 11, 2022

4. Goyal, Prateek&Mandwade, Prashant & Dutta, Sourabh. (2022). Role of Pharmaceutical Excipients in Solid Oral Dosage Forms (Tablets). 7. 46-48.

5. Saito, J.; Agrawal, A.; Patravale, V.; Pandya, A.; Orubu, S.; Zhao, M.; Andrews, G.P.; PetitTurcotte, C.; Landry, H.; Croker, A.; et al. The Current States, Challenges, Ongoing Efforts, and Future Perspectives of Pharmaceutical Excipients in Pediatric Patients in Each Country and Region. Children 2022, 9, 453. https://doi.org/ 10.3390/children9040453 Academic Editor: KarelAllegaert Received: 10 February 2022 Accepted: 18 March 2022 Published: 23 March 2022

6. Van den Anker, J.; Reed, M.D.; Allegaert, K.; Kearns, G.L. Developmental Changes in Pharmacokinetics and Pharmacodynamics. J. Clin. Pharmacol. 2018, 58, S10–S25

7. Walsh, J.; Ranmal, S.R.; Ernest, T.B.; Liu, F. Patient acceptability, safety and access: A balancing act for selecting age-appropriate oral dosage forms for paediatric and geriatric populations. Int. J. Pharm. 2018, 536, 547–562.

8. European Medicines Agency (EMA). Questions and Answers on Benzoic Acid and Benzoates Used as Excipients in Medicinal Products for Human Use; EMA: London, UK, 2014. Available online: https://www.ema.europa.eu/en/documents/scientificguideline/questions-answers-benzoic-acid-benzoates-used-excipients-medicinal-products-human-use_en.pdf (accessed on 2 February 2022).

9. Ohio Northern University. Pharmacist Role in Managing Special Patient Needs Related to Excipients; Medical Association; Ohio Northern University: Ada, OH, USA, 2009. Available online: https://apps.who.int/medicinedocs/en/d/Jh2995e/1.6.2.html (accessed on 2 February 2022).

10. Andersen, A. Final amended report on the safety assessment of methylparaben, ethylparaben, propylparaben, isopropylparaben, butylparaben, isobutylparaben, and benzylparaben as used in cosmetic products. Int. J. Toxicol. 2014, 27, 1–82.

11. Walsh, J.; Cram, A.; Woertz, K.; Breitkreutz, J.; Winzenburg, G.; Turner, R.; Tuleu, C. Playing hide and seek with poorly tasting paediatric medicines: Do not forget the excipients. Adv. Drug Deliv. Rev. 2014, 73, 14–33.

12. Rouaz, K.; Chiclana-Rodríguez, B.; Nardi-Ricart, A.; Suñé-Pou, M.; Mercadé-Frutos, D.; Suñé-Negre, J.M.; Pérez-Lozano, P.; García-Montoya, E. Excipients in the Paediatric Population: A Review. Pharmaceutics 2021, 13, 387.

13. Belayneh, A.; Tadese, E.; Molla, F. Safety and biopharmaceutical challenges of excipients in off-label pediatric formulations. Int. J. Gen. Med. 2020, 13, 1051–1066.

14. British Medical Association and Royal Pharmaceutical Society of Great Britain. General Guidance: Excipients. In Joint Formulary Committee; British National Formulary 2013–2014 Edition; British Medical Association and Royal Pharmaceutical Society of Great Britain: London, UK, 2014.

15. Soremekun, R.; Ogbuefi, I.; Aderemi-Williams, R. Prevalence of ethanol and other potentially harmful excipients in pediatric oral medicines: Survey of community pharmacies in a Nigerian City. BMC Res. Notes 2019, 12, 460.