

Overview of pharmaceutical excipients used in tablets and capsules

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The pharmaceutical industry is ever thirsty to satisfy patient's therapeutical needs and apart from active ingredients, inactive excipients play a major role in formulation development. Pharmaceutical excipients are substances other than the pharmacologically active drug or prodrug which are included in the manufacturing process or are contained in a finished pharmaceutical product dosage form.

In addition to transporting the active drug to the site in the body where the drug is intended to exert its action, excipients play an important part in the manufacturing process. They may also be important for keeping the drug from being released too early in the assimilation process in places where it could damage tender tissue and create gastric irritation or stomach upset.

Others help the drug to disintegrate into particles small enough to reach the blood stream more quickly and still others protect the product's stability so it will be at maximum effectiveness at time of use. In addition, some excipients are used to aid the identification of a drug product.

Last, but not least, some excipients are used simply to make the product taste and look better. This improves patient compliance, especially in children. Although technically "inactive" from a therapeutic sense, pharmaceutical excipients are critical and essential components of a modern drug product. In many products, excipients make up the bulk of the total dosage form (1). Apart from the drug's active ingredient, other essential components include diluents or fillers, binders, disintegrants, lubricants, coloring agents and preservatives (3). Diluents or fillers are inert ingredients that can significantly affect the chemical and physical properties of the final tablet thus affecting the biopharmaceutical profile.

One classic example of this are calcium salts, which can be utilized as fillers, which interfere with the absorption of tetracycline from the gastrointestinal tract. (4) This example emphasizes that excipients may not always be inert, as they may be perceived.

Usually tablets are designed so that the smallest tablet size which can be conveniently compressed is formed. Thus, if the dose is small more diluents are required and if the dose is high less diluents are required as not to increase the tablet size, which might make it difficult to swallow.

Diluents selection should be made carefully as physical-chemical changes might render the product unstable and might cause problems in manufacturing. Binders are added to tablet formulations to add cohesiveness to powders thereby providing the necessary bonding to form granules which under compaction form a compact mass as tablet. In other words, binders are essential to achieve the "hardness" of the tablet.

Binders are usually selected on basis of previous experience, particular product needs, literature or vendor data or the preference of individual scientists or manufacturing unit. The primary criterion when choosing a binder is its compatibility with other tablet components.

It must add sufficient cohesion to the powders to allow for normal processing yet allow the tablet to disintegrate and the drug to dissolve upon ingestion, releasing the active ingredients for absorption. Disintegrants facilitate the breakup of a tablet after oral administration.

They can be added prior to granulation or during the lubrication step prior to compression or at both processing steps. The effectiveness of many disintegrants is affected by their position within the tablet. Since disintegration is the opposite operation to granulation (agglomeration) and the subsequent formation of strong compacts, one must carefully weigh these two phenomena when designing a tablet. Lubricants prevent sticking of the tablets to the tablet punches during the compression phase of the tablet manufacturing process.

When lubricants are added to a powder mass, they form a coat around individual particles which remains more or less intact during compression. Lubricants are mostly hydrophobic. The presence of lubricant coating may cause an increase in the disintegration time and a decrease in drug dissolution rate. The choice of a lubricant may depend upon the type of tablet being manufactured, dissolution, flow characteristics and requirements of the formulation in terms of hardness, friability and compatibility. Glidants are the materials that have good flow properties and poor lubrication properties.

Glidants improve the flow of powder into the tableting machines for compaction. They act to minimize the tendency of a granulation to separate or segregate due to excessive vibration. High speed tablet machine require smooth even flow of material to die cavities (tablet mold). The uniformity of tablet weights directly depends on how uniformly the die cavity is filled. In general many materials commonly referred to as lubricants possess only a minimal lubricating activity and are better glidants or anti-adherents.

Thus a blend of two or more materials may be necessary to obtain these properties. Pharmacists should be familiar with the components of pharmaceuticals products, beyond their active ingredients. In order to educate pharmacists on excipients that are routinely used in the pharmaceutical industry, we decided to examine the top 200 prescription tablets and capsules products of 2003 (2) and find out how many or which excipients are used in each product.

The selection will cover both brand and generic drugs. Out of the 200 prescription drugs, the total numbers of inactive excipients used except for coating and coloring agents were ONLY 94! Although the list is composed on the top 200 drugs of 2003, very few blockbusters has been launched since then and still the excipients in all remains the same.

No:	Excipient	Number of times excipients used in tablets out of 200	Use
1	Acacia	2	Emulsifying agent; stabilizing agent; suspending agent; tablet binder; viscosity-increasing agent
2	Alginate	1	Binder
3	Alginic Acid	1	Stabilizing agent; suspending agent; tablet binder, tablet disintegrant; viscosity-increasing agent.
4	Aluminum Acetate	1	Antiseptic
5	Benzyl Alcohol	2	Antimicrobial preservative;

			disinfectant; solvent
6	Butyl Paraben	1	Antimicrobial preservative
7	Butylated Hydroxy Toluene	1	Antioxidant.
8	Citric acid	1	Disintegrant
9	Calcium carbonate	1	Tablet and capsule diluent; therapeutic agent
10	Candelilla wax	4	Binder
11	Croscarmellose sodium	22	Tablet and capsule disintegrant
12	Confectioner sugar	1	Sugar coating adjunct; sweetening agent; tablet and capsule diluents
No:	Excipient	Number of times excipients used in tablets out of 200	Use
13	Colloidal silicone dioxide	22	Adsorbent; anticaking agent; emulsion stabilizer; glidant; suspending agent; tablet disintegrant; thermal stabilizer; viscosity-increasing agent.
14	Cellulose	19	Adsorbent; suspending agent; tablet and capsule diluent; tablet disintegrant. (cellulose microcrystalline)

			Adsorbent; glidant; suspending agent; tablet and capsule diluent; tablet disintegrant (cellulose powdered) Tablet and capsule diluent. (cellulose Silicified)
15	Plain or anhydrous calcium phosphate	3	Diluent
16	Carnauba wax	12	Binder
17	Corn starch	17	Binder
18	Carboxymethylcellulose calcium	3	Stabilizing agent; suspending agent; tablet and capsule disintegrant; viscosity-increasing agent; water-absorbing agent
19	Calcium stearate	5	Tablet and capsule lubricant
20	Calcium disodium EDTA	1	Chelation
21	Copolyvidone	1	Film-former; granulating agent; tablet binder
22	Castor oil hydrogenated	4	Extended release agent; stiffening agent; tablet and capsule lubricant
No:	Excipient	Number of times excipients used in tablets out of 200	Use
23	Calcium hydrogen phosphate dihydrate	1	Diluent
24	Cetylpyridine chloride	1	Antimicrobial preservative; antiseptic; cationic surfactant; disinfectant; solubilizing agent; wetting agent
25	Cysteine HCL	1	Reducing Agent
26	Crosspovidone	20	Tablet disintegrant.

27	calcium phosphate di or tri basic	7	Tablet and capsule diluent Anticaking agent; buffer, nutrient; dietary supplement; glidant; tablet and capsule diluent and clouding agent(for calium phosphage tribasic)
28	Dibasic Calcium Phosphate	9	Diluent
29	Disodium hydrogen phosphate	1	Buffering agent
30	Dimethicone	1	Antifoaming agent; emollient
31	Erythrosine Sodium	2	Color
32	Ethyl Cellulose	3	Coating agent; flavoring fixative; tablet binder; tablet filler; viscosity-increasing agent.
33	Gelatin	14	Coating agent; film-former; gelling agent; suspending agent; tablet binder; viscosity-increasing agent
34	Glyceryl monooleate	2	Nonionic surfactant
No:	Excipient	Number of times excipients used in tablets out of 200	Use
35	Glycerin	3	Antimicrobial preservative; emollient; humectant; plasticizer; solvent; sweetening agent; tonicity agent

36	Glycine	1	Tonicity
37	Glyceryl monostearate	1	Emollient; emulsifying agent; solubilizing agent; stabilizing agent; sustained-release ingredient; tablet and capsule lubricant
38	Glyceryl behenate	1	Coating agent; tablet binder; tablet and capsule lubricant
39	Hydroxy propyl cellulose	25	Coating agent; emulsifying agent; stabilizing agent; suspending agent; tablet binder; thickening agent; viscosity-increasing agent.
40	Hydroxyl propyl methyl cellulose	45	Coating agent; film-former; rate-controlling polymer for sustained release; stabilizing agent; suspending agent; tablet binder; viscosity-increasing agent.
41	Hypromellose	7	Coating agent; film-former; rate-controlling polymer for sustained release; stabilizing agent; suspending agent; tablet binder; viscosity-increasing agent.
42	HPMC Pthalate	1	Coating agent.
No:	Excipient	Number of times excipients used in tablets out of 200	Use
43	Iron oxides or ferric oxide	15	Color
44	Iron oxide yellow	5	Color
45	Iron oxide red or ferric oxide	6	Color

46	Lactose hydrous or anhydrous or monohydrate or spray dried	77	<p>Binding agent; diluent for dry-powder inhalers; lyophilization aid;</p> <p>tablet binder; tablet and capsule diluent.(lactose anhydrous) Binding agent; diluent for dry-powder inhalers; tablet binder;</p> <p>tablet and capsule diluent(lactose monhydrate) Binding agent; diluent for dry-powder inhalations; tablet and capsule diluent;</p> <p>tablet and capsule filler. (lactose spray dried)</p>
47	Magnesium stearate	108	Tablet and capsule lubricant
48	Microcrystalline cellulose	61	Adsorbent; suspending agent; tablet and capsule diluent; tablet disintegrant same as cellulose see above it is just that mcc is usp
49	Mannitol	4	<p>Sweetening agent; tablet and capsule diluent; tonicity agent;</p> <p>vehicle (bulking agent) for lyophilized preparations</p>
No:	Excipient	Number of times excipients used in tablets out of 200	Use
			Coating agent;

50	Methyl cellulose	3	emulsifying agent; suspending agent; tablet and capsule disintegrant; tablet binder; viscosity- increasing agent
51	Magnesium carbonate	2	Tablet and capsule diluent
52	Mineral oil	3	Emollient; lubricant; oleaginous vehicle; solvent
53	Methacrylic acid copolymer	5	Coating
54	Magnesium oxide	2	Tablet and capsule diluent
55	Methyl paraben	5	Antimicrobial preservative
56	Povidone or PVP	36	Disintegrant; dissolution aid; suspending agent; tablet binder.
57	PEG	40	Ointment base; plasticizer; solvent; suppository base; tablet and capsule lubricant
58	Polysorbate 80	19	solubilizer
59	Propylene glycol	10	Antimicrobial preservative; disinfectant; humectant; plasticizer; solvent; stabilizer for vitamins; water-miscible cosolvent.
60	Polyethylene oxide	3	Mucoadhesive; tablet binder; thickening agent.
61	Propylene paraben	4	Antimicrobial preservative
62	Polaxamer 407 or 188 or plain	3	Dispersing agent; emulsifying and coemulsifying agent; solubilizing agent; tablet lubricant; wetting agent.
63	Potassium bicarbonate	1	Alkalizing agent; therapeutic agent
No:	Excipient	Number of times excipients used in tablets out of 200	Use
64	Potassium sorbate	1	Antimicrobial preservative
65	Potato starch	1	Binder
66	Phosphoric acid	1	Acidifying agent
67	Polyoxy140 stearate	1	Emulsifying agent; solubilizing agent;

			wetting agent
68	Sodium starch glycolate	20	Tablet and capsule disintegrant
69	Starch pregelatinized	21	Tablet and capsule diluent; tablet and capsule disintegrant; tablet binder (starch pregelatinized Glidant; tablet and capsule diluent; tablet and capsule disintegrant; tablet binder.(starch , potato, corn , wheat, rice) so check the above and make the changes
70	Sodium crossmellose	1	Disintegrant
71	Sodium lauryl sulfate	13	Anionic surfactant; detergent; emulsifying agent; skin penetrant; tablet and capsule lubricant; wetting agent
72	Starch	19	Glidant; tablet and capsule diluent; tablet and capsule disintegrant; tablet binder.(starch , potato, corn , wheat, rice) combine all the starches
73	Silicon dioxide	14	Same as colloidal silicon dioxide
No:	Excipient	Number of times excipients used in tablets out of 200	Use
74	Sodium benzoate	2	Antimicrobial

			preservative; tablet and capsule lubricant
75	Stearic acid	12	Emulsifying agent; solubilizing agent; tablet and capsule lubricant.
76	Sucrose	9	Base for medicated confectionery; granulating agent; sugar coating adjunct; suspending agent; sweetening agent; tablet and capsule diluent; viscosity-increasing agent.
77	Sorbic acid	3	Antimicrobial preservative
78	Sodium carbonate	1	Carbonating agent
79	Saccharin sodium	1	Sweetening agent
80	Sodium alginate	1	Stabilizing agent; suspending agent; tablet and capsule disintegrant; tablet binder; viscosity-increasing agent.
81	Silica gel	1	Adsorbant
82	Sorbiton monooleate	1	Solubilizer
83	Sodium stearyl fumarate	4	Tablet and capsule lubricant.
84	Sodium chloride	3	Tablet and capsule diluent; tonicity agent
85	Sodium metabisulfite	1	Antioxidant.
86	Sodium citrate dihydrate	1	Alkalizing agent; buffering agent; emulsifier; sequestering agent.
87	Sodium starch	1	Binder
88	Sodium carboxy methyl cellulose	1	Coating agent; tablet and capsule disintegrant; tablet binder; stabilizing agent; suspending agent; viscosity-increasing agent; water-absorbing agent.
No:	Excipient	Number of times excipients used in tablets out of 200	Use
89	Succinic acid	1	Acidity
90	Sodium propionate	1	Antimicrobial preservative
91	Titanium dioxide	49	Coating agent; opacifier; pigment

92	Talc	20	Anticaking agent; glidant; tablet and capsule diluent; tablet and capsule lubricant.
93	Triacetin	6	Humectant; plasticizer; solvent
94	Triethyl citrate	3	Plasticizer

From the table above we see that most of the commonly used ingredients have not been changed in making a tablet from generations and might follow the same trends for many generations to come.

CONCLUSION: Lot of time and effort are still needed in field of excipients. However till then a formulation scientist is entrusted with the limited amount of excipients and will have to deal with 94 excipients or now maybe 104.

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