

A SYSTEMATIC REVIEW OF THE APPLICATION OF NATURAL POLYMERS IN THE FORMULATION OF ORO-DISPERSIBLE TABLET

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Received: 25 Apr 2023, Revised and Accepted: 06 Jul 2023

ABSTRACT

Oral drug delivery is still the preferred method for administering many medications. Recent technological advancements have led to the development of orally disintegrating drugs, which offer improved patient compliance and convenience. Orodispersible (ODTs) drugs are a unique dosage form that dissolves in the mouth within 1-3 min without the need for chewing or water. Over the past three decades, orodispersible drugs have gained popularity as an alternative to traditional drugs due to their increased patient compliance, solubility, and stability. This new technology meets both the pharmaceutical and patient demands and provides a comfortable dosage method for pediatric, geriatric, and psychiatric patients with dysphagia. Natural substances are preferred over synthetic ones because they are more accessible, less expensive, non-toxic, and chemically inert. Natural polymers, such as locust bean gum, banana powder, mango peel pectin, and *Mangifera indica* gum, enhance drug characteristics and are used as binders, diluents, and super disintegrants to speed up disintegration, increase solubility, and provide supplements. Manufacturers are increasingly using natural polymers due to various issues with medication release and adverse effects. This review article views the development of ODTs, challenges in formulation, new ODT technologies, and our suspects.

Keywords: Oral drug transport, Orodispersible tablets, Conventional tablets, Natural polymers

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INTRODUCTION

Oral drug transport continues to be the desired approach to administration. Scientists have created orally disintegrating pills with elevated affected person compliance and comfort as a result of the latest technological advancements [1, 2]. The course offers clean, simplicity of medicine administration, and sufferers are greater used to it. Therefore, compared to opportunity modes of administration, together with parenteral, oral medicinal drug transport frequently outcomes in extra affected person compliance and, consequently, greater a hit drug therapy. There is sizable proof that oral transport can provide equivalently exceptional scientific outcomes, has fewer problems, is much less expensive, and inconveniences sufferers much less [3-5]. Now a day the most effective technique is Oro dispersible tablets. These Oro dispersible are mouth-dissolving pills, brief disintegrating, speedy dissolving, speedy dissolving, porous, and speedy melts. ODT is a stable dosage shape containing a medicinal drug or energetic factor that quickly, regularly in more than one second, while placed on the tongue, in line with America Food and Drug Administration. ODTs normally crumble in a time frame between some seconds and a minute or greater [6].

The inclusion of tremendous disintegrants, along with cross-connected which allows speedy disintegration while entering into alternate with water or salivary secretions, distinguishes ODTs from different dental techniques. Drug bioavailability can also additionally growth because of oral and pregastric administration. As a result, compared to conventional dose forms, drug dispersion and absorption as well as the beginning of scientific motion, can be accomplished [7, 8].

Three years ago, an orodispersible tablet has been tested to be a powerful dose. Orodispersible movies also are utilized in numerous experimental designs for brief dissolution, along with the Box-Behnken statistical design [9-11]. There are many exceptional drug shipping systems; however, present-day traits in novel drug delivery system purpose to enhance affected person compliance even as enhancing the protection and efficacy of healing molecules via way of means of growing a handy dosage shape for administration. Lead to orodispersible pills is one method [12, 13].

A thorough literature analysis was carried out by looking through pertinent publications from peer-reviewed journals that were found online in databases like Scopus, Google, Google Scholar, Mendeley,

Springer Link, Research Gate, PubMed, and Shodhganga. Libraries of the CD Bioparticles Drug Delivery, Natural Polymer Chemical Research Group, Polymer Science and Technology, CSIR, Natural Polymer and Biomimetics, CiMUS, Polymer Processing Research Centre. Utilising keywords like polymer, natural polymers, polymer synthesis, polymerization, polymer characterization, application of polymer, properties of polymer, polymer processing, natural polymer sources, orodispersible tablets, conventional tablets. Based on the titles and abstracts, the authors did a preliminary review of the papers, finding 164 entries in databases and 32 records from other sources. Also performed the descriptive literature review from year 1990 to 2023. Studies describing the usage of polymer for therapeutic purposes were the only ones included; those describing just views, attitudes, or beliefs of people or groups regarding the therapeutic drug delivery potential were included.



Fig. 1: Components of orodispersible tablets

ODT challenges

The development of ODTs and other orodispersible dosage forms is complicated by taste masking. The difficulty of masking the taste of unpleasant medications or the lack of appropriate *in vitro*/preclinical taste evaluation procedures serve as examples of the challenge [14].

Taste-masking approaches

The difficulty of giving medications with a bitter taste as the tablet dissolves in the mouth is one of the frequent problems with ODTs [14]. Furosemide's flavour was concealed by granulating the other excipients with yogurt (sour) or maltitol (sweet) powder added as flavour modifiers. This approach is often easy to design and depends on how much flavor used is to reduce the bitter and unpleasant taste. Yet, certain medications must be taste-masked by coating (spray coating), encapsulating via spray drying, or a complexation technique since they are quite bitter [15].

There are particular requirements for taste-masking techniques that put a physical barrier between the medicine and the tongue's taste buds. They are either process-related characteristics, like the taste-masking approach's cost-effectiveness and scalability, or product-related characteristics. One of the traditional methods that might provide a physical barrier between the medication and the tongue's taste buds is spray coating. Either a fluidized bed, which uses a spray gun to atomize the coating polymer and a stream of air to disseminate the medication, or pan coating, using a spray gun is used to apply the coating to the drug particles. In one coating technique, a coating polymer that slows oral dissolution was sprayed over the core, which might include the medicine, a sweetener, and a binder. To get the coated microparticles, this was followed by drying [16]. Low compression force was used to compress the microparticles into ODT to prevent coating layer fracture and consequent drug leakage.

Taste assessment approaches

The majority of human panel volunteers that participate in the taste evaluation of ODTs taste the tablet before and after it has completely disintegrated [17]. The approach itself offers the most accurate data on ODT flavour and aftertaste; nevertheless, the expenses involved with finding and preparing healthy volunteers. Drug release studies are frequently used as a deceptive technique for evaluating taste by determining if a formulation may impede drug release in a mouth-simulated environment. The primary drawback of this approach is the dearth of accurate information on flavour and/or intensity of taste. For instance, a formulation that fails to utilize the drug release strategy may still include a little quantity of a bitter component that is adequately offset by the addition of sweeteners or other flavour modifiers. The invention of synthetic taste sensors, sometimes known as electronic tongues, was an intriguing advance. They use chemometrics software in conjunction with electrochemical sensors to distinguish between tastants [18]. Electronic tongues are said to make little consideration for the physiological circumstances in the mouth, making it challenging to make definitive claims about the taste of a particular substance [19]. Also, the price of analysis utilizing these tools is rather costly. Other strategies, such as physiological procedures or cell culture, or evaluating animal preferences, are currently being developed.

Poorly soluble medicines are dissolved and then included into ODTs

Given that approximately 40% of the medications in the pipeline for research are just marginally water-soluble, improving the solubility of pharmaceuticals packaged into ODTs has become an increasingly relevant topic [20]. Solid dispersion and milling are the two most often used solubilization methods for ODTs. Poorly water-soluble medicines are transported via the solid dispersion approach using hydrophilic excipients like polyvinyl pyrrolidone (PVP) and PEG. Drug particles may be inserted into the matrix of the carrier polymer by blending the poorly soluble drug with it using an appropriate dispersion process. Usually, higher amorphous or better wettability brought on by the carrier polymer's wicking action boosts the drug's ability to dissolve. A combination of hot-melt extrusion, milling, and the solvent evaporation process was used to create the solid dispersions for ODTs described in the literature. Rofecoxib, a poorly soluble medication, was made into a solid dispersion with PVP using the solvent evaporation technique [21].

Limited dose capacity for ODTs

Harman *et al.*, (2007) reported that "One of the problems with first-generation ODTs made by freeze drying is their extremely low

dosage capacity (50 mg for water-soluble medicines), as greater doses may affect the compact's hardness. Similar to ODTs, compression-produced ODTs have a maximum dosage capacity that is close to 30–40% of the tablet's weight. This is significant since it limits the usage of ODTs to low-dose medications exclusively" [22]. According to US FDA recommendations, unless the ingredients are substantially water soluble, the total ODT weight should not exceed 500 mg [23]. Crowley *et al.*, (2013) reported that "This poses an extra problem since it would change the amount of an insoluble excipient or poorly soluble medicine to be utilized in an ODT. However, when employing some of the present ODT methods and high-dose medications like acetaminophen, the ultimate weight of the ODT may reach 750 mg-1 g. Moreover, bitter-tasting medications experience a similar problem since taste-masking techniques (which create one or more coating layers) make the drug particle heavier and larger, which in turn affects the ODT's ultimate weight. Also, it was demonstrated that poorly soluble medicines may, when their concentration is increased, alter the disintegration time of compressed ODTs" [24]. With the increase in the number of poorly soluble medications in the drug development pipeline, this issue is more important.

Development of fast disintegrating ODTs with modified release kinetics

Corpciogluet *et al.*, (2005) reported that "The primary areas of focus for the pharmaceutical industry and academic research are the development of technologies and the formulation of ODT base/matrix. The immediate-release characteristic of ODTs, where the dosage form swiftly dissolves in a matter of seconds, is mostly to blame for this. The rapid release is the rapid characteristic shared by all mouth-dissolving dosage forms, including chewable/sackable tablets and thin films. Pregastric absorption can occasionally enhance a drug's release when it is administered as an ODT" [25]. Alhusban *et al.*, (2011) reported that "To expand the ODT platform and enable the distribution of medications in a delayed or sustained way to achieve alternative pharmacokinetics, new supporting technologies are being integrated inside the ODT fast disintegrating base. It could be difficult to incorporate some pharmaceuticals into an existing ODT matrix without putting a coating layer, or sometimes numerous coating layers, over the drug particle or granule. Multi-articulate drug delivery methods are developed to achieve the proper pharmacokinetics. These release mechanisms enable drugs to be protected from the acidic environment of the stomach, targeted to certain regions of the intestine for enhanced absorption, given a longer duration of action, or given less often" [26].

Problems with powder flow and necessary improvements

Kasliwal *et al.*, (2011) reported that "Powders designed for ODT compression must have an adequate flowability to be handled easily during blending and processing and to permit continuous flow from the hoppers into the tablet press's die. Granulated powders used to create ODTs often have better flow properties due to their consistently large particle size and less formation of particles" [27]. Castellanos *et al.*, (2005) reported that "In contrast, powders made by mixing or processing ODTs for direct compression often have poor flowability due to their smaller particle size or greater size dispersion, non-uniform shape, and occasionally uneven surface roughness. The latter properties lead to interactions between particles that alter flow by causing electrostatic charges, Van der Waals forces, local chemical bonds, and bridging forces" [28].

Sensitivity of the lubricant and possible remedies

Zurrman *et al.*, (1999) reported that "The friction between the tablet and the machine die or punch is reduced by the application of a lubricant during tablet manufacture. Magnesium stearate is the lubricant used in the manufacturing of tablets the most frequently since it is widely available and reasonably priced. Nonetheless, it is well known that magnesium stearate, depending on how sensitive the excipients are to the lubricant, can reduce the mechanical strength of tablets" [29]. For instance, plastic-deforming materials show greater lubrication sensitivity to mixing with magnesium stearate because the excipient particles create a lubricant layer that inhibits inter-particle interaction. MCC is a popular excipient for

creating ODTs because of its strong mechanical properties and quick breakdown. The inclusion of magnesium stearate, which significantly lessens the hardness of tablets containing MCC, has a considerable impact on it, nevertheless. Also, according to some studies, magnesium stearate's hydrophobic nature might cause it to take longer for tablets to dissolve and lengthen the disintegration time.

Marketed orodispersible tablets

In the previous ten years, orodispersible tablets were introduced to the pharmaceutical industry to improve patient adherence to treatment and medication bioavailability. In addition to children and the elderly, patients with dysphagia were the main target market for this technology's application in analgesics, antiallergics, and medications to treat mental illnesses. Due to the simplification of this technology's manufacturing process and the loss of patent protection for several prescription items created using this technology, orodispersible tablets are now extensively employed in the global pharmaceutical business.

Given the benefits shown, saying that certain patients' use of the orodispersible technology may make the difference between a successful therapy and a therapeutic failure is not overstating the case. In this sense, healthcare providers, including pharmacists, doctors, nurses, and carers, must be aware of the specifics of orodispersible medicinal items so they may consider how they can improve patients' health [30].

Drugs formulated as ODT

For sufferers of a sure age and with a sure contamination state, ODTs offer a few substantial benefits over different conventional dose forms. The majority of sufferers have problem taking their medications. However, troubles and resistance to swallowing capsules are very standard and greater not unusual places amongst psychiatric pediatric and aged sufferers [31]. Therefore, ODT resources in appropriate per oral management with inside the pediatric populace whilst swallowing is an issue [31]. ODTs don't require water, making them especially sensible for visitors who're passing thru dry regions [32]. In addition to this, ODTs additionally offer effortlessly measured dosing [33]. bearing in mind correct dose measurement. The technique will increase bioavailability and affords a brief graduation of effect [34].

Desired criteria for oro dispersible tablets

- Should soften or collapse with inside the mouth in multiple seconds without the want for water to eat it [35].
- Work nicely with flavor muffling.
- Have no fragility problems at the same time as being portable.
- Feel properly within side the mouth.
- Immediately following oral administration, depart little to no residue within side the mouth.

Current ODT manufacturing trend

Orodispersible tablets are made using the techniques of lyophilization, molding, direct compression, cotton sweet process, spray drying, sublimation, and nanonization. These strategies were developed using the concepts of increasing absorbency and/or adding super disintegrants and water-soluble excipients to the formulation of the pills [36].

Techniques for preparing orodispersible tablets

Direct compression

The maximum handy and low-cost approach to creating pills. Utilizing a minimum range of processing stages, traditional compression machines are hired with primary materials. By which includes bubbling cloth in a pill to supply carbon dioxide, which additionally aids in disguising the flavor of a medicine, speedy disintegration also can be achieved. The capability of bubbling paperwork to take in air moisture, or hygroscopicity, is a prime negative. Super disintegrants can also additionally, from time to time, be delivered within side the proper quantity to create precise oral dispersibility and a pleasing sensation [37].

Lyophilization

With this pharmaceutical procedure, biologicals and prescription medications can be dried, which are touchy to warmth, through the use of a vacuum to get rid of water through sublimation. The drugs are carried out in prefabricated blister packs after being dissolved or distributed in an aqueous service solution, frozen out using a nitrogen flush, and then packaged again. The process is finished in a refrigerator after that [38]. The first-rate porosity and precise floor place of lyophilization processes, in addition to their speedy dissolution withinside the mouth and excessive drug bioavailability, are their distinguishing features. The system's important flaws are its excessive cost, labor-extensive process, and fragility, which renders conventional packaging unsuited for the use of with this dosage shape and reasons balance issues beneath neath pressure [39].

Molding

By molding, strong dispersions are created withinside the shape of drugs. Dependent on whether or not and what sort of the medicine dissolves withinside the molten provider, the drug's bodily form withinside the tablet. The drug may also exist as discrete or microscopic debris dispersed all through the matrix. It may also absolutely dissolve withinside the molten provider to shape a strong solution, or it could dissolve partly withinside the molten provider with the last particle last undissolved and dispersed all through the matrix. Depending on the type of dispersion or dissolution, disintegration time, medicine dissolving rate, and mouth experience will change. The dispersion matrix of molded drugs is frequently made out of water-soluble sugars, which reasons them to dissolve extra quickly and feature higher flavour [40]. The mechanical energy of molded drugs is commonly instead weak. Molded drugs often enjoy erosion and breaking. Typically, molded drugs do not have loads of mechanical energy. When coping with and establishing blister packets, molded drugs often erode and shatter [41, 42].

Sublimation method

The restricted porosity of the drugs is the reason for the compressed tablet's behind-schedule disintegration, even if it carries chemical substances which are particularly water-soluble. Then, the use of a completely porous matrix and sublimation separation are used to extract the unstable material. The common disintegration time for drugs created by the use of this manner is 10 to twenty seconds [43].

Spray-drying

Allen *et al.* (1996) reported that "sodium starch glycolate or croscarmellose sodium as a disintegrating agent, hydrolyzed and nonhydrolyzed gelatines as binding agents, mannitol as a bulking agent, citric acid or sodium bicarbonate to sell dissolution, and sodium starch glycolate croscarmellose sodium as a disintegrating agent" substances are blended on this way. When a dosage shape comes into touch with an aqueous medium the usage of the spray-drying method, the dosage shape dissolves quickly (within 20 seconds) [44, 45].

Nanonization

It consists of using moist grinding to lessen particle length to the nano variety. The created nanocrystals are then bodily connected to the floor of an inert substance to stabilize them and keep them away from agglomeration. This method's blessings consist of being cost-effective, being capable of tolerating stress, and preserving an extensive variety of dosages (as much as two hundred mg). It is likewise best for medicinal drugs that aren't water-soluble and feature a low bioavailability [46].

Cotton candy

By simultaneously spinning and flash melting, a matrix of polysaccharides is fashioned on this technique [47]. The matrix is then partly or recrystallized, generating a fabric with ideal glide and compressibility characteristics. The candyfloss can then be compacted into ODT after being pulverized, pulverized, and combined with lively materials and different excipients. The employment of this technique is, however, limited to thermostable chemical compounds most effective because of the excessive processing temperature [48].

Fast dissolving films

Bees reported that "It consists of a drug and every other taste-protecting agent which can be used to broaden a movie because the solvent evaporates. The nonaqueous answer consists of water-soluble movie-forming polymers (pullulan, carboxymethyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose polyvinyl pyrrolidone, polyvinyl alcohol, or sodium alginate). Resin adsorbate or covered microparticles of a medication may be hired in a movie while a drug has an unsightly taste. These tiny movies have dimensions of two inches with the aid of using 2 inches and fall apart fast in five seconds" [49].

Compaction

By including hydrophilic waxy binder (first-rate polystrate) PEG-6-stearate, soften granulation is created. This binder has a twin function, improving disintegration whilst concurrently improving bodily strength. Such dose bureaucracy makes it easy to supply medicines like griseofulvin. The compaction technique has the function of melting fast within the mouth and leaving no trace [50].

Orodispersible tablet innovations covered by patents

Several patented technologies were created to create Oro dispersible tablets, and they are as follows:

Zaydis technology

The proprietor of the Zaydis technique is Scherer, a department of Cardinal Health. By incorporating the lively remedy right into a water-soluble matrix that eventually becomes a blister wallet and freeze-dried to dispose of water through sublimation, this method employs freeze-drying to create tablets. To provide the matrix its energy during handling, gelatine, dextran, or alginates are utilized mannitol or sorbitol is given to give it crystallinity, elegance, and hardness; and specialized gums can be used to prevent the settling of drug debris that has been dispersed [51].

Oraquick technology

A proprietary taste-covering method is used with inside the method of Oraquick fast-dissolving/disintegrating tablets. Since there aren't any solvents used in this flavour covering procedure, production is speeded up and made greater effective. This approach is suitable for medicinal drugs, which might be touchy to warmness seeing that low warmness is created at some stage in processing. Microencapsulated particle is allegedly greater malleable, consistent with KV Pharmaceuticals. This approach produces tablets that quickly dissolve and cover awful tastes in multiple seconds [51].



Fig. 2: Objective of oro dispersible tablets

Shear form technology

The basis of this method is the advent of floss, additionally recognized as "Shear form Matrix," which is made through filing a feedstock that carries a sugar in service to flash warmness processing. Due to the amorphous nature of the floss created in this manner, it's far similarly diced and recrystallized. The re-crystallized matrix is in the end blended with an energetic aspect and extra pill excipients. Tablets are created by compressing the mixture [52].

Nanocrystal technology

The Prussian king Elan is the inventor of this. The lyophilisation of colloidal medicinal cloth dispersions and water-soluble additives located in the blister wallet is part of nanocrystal technology. This technique does now no longer use production steps like granulation, mixing, and tableting, which is higher for risky and robust medicines. This technique works properly for modest quantities of drugs on account that manufacturing losses are minimal [53].

Industrial applications

- To create oral disintegrating dose paperwork and collaborate with already-to-be-had disintegrants
- To similarly expand the ODTs' modern technology
- To acquire ODTs by optimizing the aggregate of excipients or disintegrants
- Select and create suitable packaging substances and structures for accelerated product balance in addition to creating a product this is affordable.
- To expand best transport techniques and taste-protecting agents to enhance affected person compliance.
- To create disintegrants from numerous polymers, which might be changed to be hired as coating substances and used to create ODTs [54].

Advantages of formulating oro dispersible tablets

Oro dispersible drugs have the gain of being easy to supply to sufferers with swallowing issues, inclusive of the elderly, stroke sufferers, and younger children. As a result, the bedridden affected person will comply greater, rather than a traveler who can also additionally have a constrained get right of entry to the water. Drugs having a nice mouthfeel can also additionally make contributions to a mental perception in remedy this is strengthened. Ease of management to sufferers of all ages [55]. Drugs are greater quickly and punctiliously absorbed from pre-gastric quantities of the GIT, which will increase their bioavailability and effectiveness [56]. Cost-powerful due to the fact only a few additives are needed. superior protection with the aid of using avoidance of choking or blockage whilst swallowing, as in the case of traditional dose forms [57]. Disperse or dissolve remedy the use of a stable dose form [58].

Natural polymers

A large molecule (macromolecule) made of repetitive structural gadgets is called a polymer. Covalent chemical bonds are regularly used to sign up for those subunits. Both artificial and herbal polymers are available, but due to the fact they may be affordable, broadly accessible, and non-toxic, herbal polymers are extra attractive to be used in pharmaceutical applications. With some exceptions, they may be additionally biocompatible, chemically modifiable, and possibly biodegradable [59].

Biologically derived polymers, inclusive of the ones from vegetation and animals. They are found in all residing matters and assist the metabolic procedures in each vegetation and animal. In each kingdom, herbal polymers function constructing blocks for preservation and bodybuilding. They can be located anywhere and are omnipresent. For instance, rubber, cellulose, etc. Natural polymers like carbohydrates, proteins, and different substances make up herbal meals. Polymers also are used to make meals, transport containers, packs, single-use cutlery, and different items [60-65].

Table 1: Application of natural polymer and formulation

S. No.	Drug	Natural polymer	Formulation	Reference
1.	Insulin	Chitosan	Ionic gelation	91
2.	Enoxaparin (low molecular weight heparin)	Alginate-chitosan	Ionic gelation	92
3.	Curcumin	Galactosylated	Ionic gelation	93
4	Leguminan DNA vaccine	Alginate-chitosan	Stirring method	94
5	Doxorubican	Alginic acid	Counterion complexation	95
6	Tetracycline	Alginic acid	Cation-induce controlled gelification	96
7	Bupropion HCl	Agar	Ionic cross-linking	97
8	Piroxicam	Ethylcellulose	Solvent evaporation	98
9	Acyclovir	Carboxymethyl cellulose acetate butyrate	Conventional precipitation and rapid precipitation	99
10	Theophylline	Collagen	Electrospray deposition	100
11	DNA	Gelatin	Precipitation	101
12	Itraconazole	Pectin	High pressure Homogenization	102
13	Platinum Complex	B-lactoglobulin-pectin	Complexation	103
14	Methotrexate	Pectin	Iontropic gelation	104
15	Flutamide	Casein	O/w emulsification	105
16	Carbazole	Gliadin	Desolvation	106
17	Dexorubican	Silk	Modified dissolution	107
18	Epirubicin	Cholesterol-modified pullan	Self-aggregation	108

Need for natural polymers

- Biodegradable-All dwelling matters make going on polymers. They don't seem to have any poor effects on human beings or the environment.
- Economically, they outperform artificial substances in phrases of fees and production costs.
- Safe and without aspect effects-Because they arrive from an herbal source, they're each secure and freed from unfavourable reactions.
- Easy accessibility-Because they're utilized in such a lot of distinctive sectors, they're produced in lots of distinctive nations [66].

Natural polymers used in orodispersible tablets

When proven to be secure and biocompatible, the usage of herbal polymers is advantageous. Because they may be low priced and broadly every day through regulators, herbal gums are a number of the maximum broadly used hydrophilic polymers. In floating drug transport systems, polymers are regularly used to direct medicinal drug transport to the stomach, a selected location of the gastrointestinal tract. These polymers can also be changed chemically and create gels, and they may be secure and harmless [67].

Chitin and chitosan

Bruscato and Danti, 1978, found out that irrespective of the drug's solubility, whilst chitin became delivered to standard tablets, the drugs dissolved within five to ten minutes. Surface unfastened power can be used to observe each the wetting time and the disintegration time within side the oral cavity. The maximum famous herbal polysaccharide used withinside the pharmaceutical quarter is chitosan, which has a huge variety of uses [68].

Cellulose

Cellulose, hemicelluloses, and pectin make up the bulk of the plant's mobileular wall's polysaccharides [69]. The maximum usual natural polymer on earth, cellulose is an essential structural detail of better plant molecular walls. Crystalline microfibrils manufactured from numerous parallel cellulose molecules are each extraordinarily proof against enzyme attack and automatically robust. These are covered up with each other to present the molecular wall structure. Cellulose can not be digested with the aid of using people and isn't soluble in water [70, 71]. Applications for cellulose derivatives in managed launch encompass the introduction of monolithic matrix structures or membrane-managed drug launch structures. Enteric-lined dosage paperwork and using semipermeable membranes in osmotic pump shipping structures are movie coating strategies used withinside the manufacturing of membrane-managed launch structures [72].

Guar gum

Guar gum is manufactured from the endosperm of the seed of the guar plant, *Cyamopsis tetragonoloba (L) Taub*, and is typically composed of galactomannans-derived polysaccharides with extremely high molecular weights (about 50,000-8,000,000). (Syn. *Cyamopsis psoralioides*). It is utilized as an emulsifier, stabilizer, and thickener in most worldwide locations at some point in the industry. It is a gum that happens naturally (advertised below the change called Jaguar). It is an impartial polymer made from sugar gadgets this is free-flowing, absolutely soluble, and accepted to be used in food. It isn't stricken by the pH, the quantity of moisture, or the solubility of the pill matrix. It isn't always perfectly white and occasionally becomes off-white or tan, and it has a propensity to discolour over time in alkaline settings [73].

Table 2: Natural polymer used in orodispersible tablets

S. No.	Brand name	Polymers	Concentration	Disintegration time
1	Cinnarizine	Chitosan and Chitin	3%w/w	60 sec
2	Theophylline	Agar treated agar	1-2%w/w	20 sec
3	Aceclofenac	Aeglemarmelos gum	6%w/w	8-18 min
4	Glipizide	Guar gum	1%w/w	30 sec
5	Metronidazole	Gellan gum	4%w/w	155 sec
6	GranisetronHCl	Plantago ovate seed mucilage	5%w/w	17.10 sec
7	Nimesulide	Lepidium sativum	10%w/w	17 sec
8	Aceclofenac	Mango peel pectin	0.1-4%w/w	11.59 sec
9	Lornoxicam	Soy polysaccharide	8%w/w	12 sec
10	OndansetronHCl/propranolol	Dehydrated banana powder	6%w/w	15-36 sec
11	Nimesulide	Lepidium sativum mucilage	5-15%w/w	17 sec
12	Aceclofenac	Hibiscus rosa-sinensis	6%w/w	20 sec
13	Amlodipine, granisetron hydrochloride	Gum Karaya	4%w/w	17.10 sec
14	Metformin Hcl, Paracetamol	Mangiferaindica gum	6%w/w	3-8 min
15	Metformin hydrochloride	Fenugreek seed mucilage	4%w/w	15.6 secs
16	Nimesulide	Locust bean gum	10%w/w	13 sec

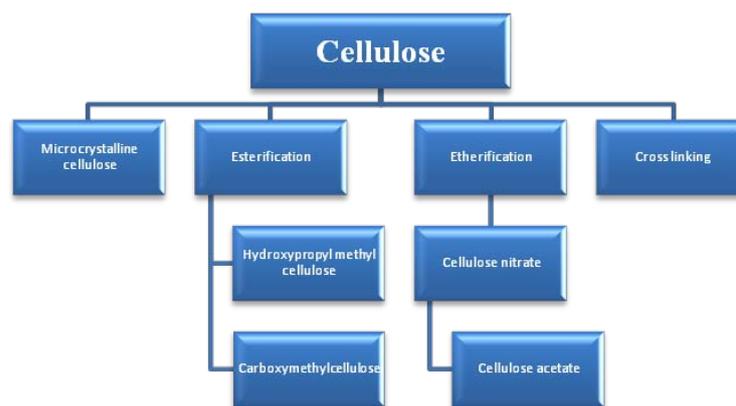


Fig. 3: Cellulose derivatives

Agar agar

The red algae *Gracilariaceae*, *pterocladia*, and *gelidiummansii* (Gelidaceae) are used to create the dried gelatinous substance known as agar-agar s(Gelidaceae). Agar is created by combining agarose with agarpectin. Agarose, the repeating monomeric unit of agarose, is the primary constituent of a linear polymer. Agarobiose is a disaccharide made up of D-galactose and 3,6-anhydro-L-galactopyranose [74]. Agar is made comprised of the polysaccharides agarose and agar pectin. Agarose gives a gel its strength, while agar pectin gives agar solutions their viscosity. Agar is a possible disintegrants candidate due to its high gel vigor [75].

Gellan gum

One of the glucose residues has acetate and glycerate substituents in its herbal or excessive acyl state. Another anionic polysaccharide with a comparable application profile to alginate is gellan gum. Transparent, heat-resistant gels crafted from gellan gum are easy to make. Gellan gum can be injected into tissues and isn't always cytotoxic [76].

Antony and Sanghavi 1997 reported that "The effectiveness of the gum turned into in comparison with that of different not unusual placed disintegrants, inclusive of dried corn starch, Explotab, Avicel (pH 10.2), Ac-di-sol, and Kollidon CL. Tablet disintegration can be a result of Gellan gum's instantaneously swelling houses and excessive hydrophilic nature whilst it comes into touch with water. The tablet's whole disintegration has set itself up as an advanced disintegrant" [77].

Lepidium sativum mucilage

Lepidium sativum, additionally called Asaliyo, belongs to the Cruciferae'scircle of relatives and is a generally used natural treatment in India. It is less expensive and usually available on the market. Used elements consist of leaves, roots, seeds, oils, and more. Different functions of Lepidium sativum mucilage consist of binding, dissolving, gelling, and more [78].

Xanthan gum

Consequences withinside the manufacturing of xanthan gum, an extracellular polysaccharide with excessive molecular weight. In one of the studies, xanthan gum outperformed artificial hydroxypropyl methylcellulose in phrases of its ability to put off the discharge of the medicinal drug. Diltiazem HCl changed launch drugs had been created by the usage of hydrophilic matrix marketers, including xanthan gum and hydroxypropyl methylcellulose. The quantity of xanthan gum had a huge effect on how tons of medicinal drugs could pop out of the direct compression drugs. It became decided that the essential changed drug launch can be executed with the aid of using making use of the ideal aggregate of hydroxypropyl methylcellulose and xanthan gum [79].

Carrageenan's

Irish moss, a pink alga derived from *Chondrus Crispus*, is some other call for the sulphated polysaccharide extract referred to as carrageenan (Rhodophyceae) [80]. Carrageenans had been

examined for their capability to compact, and the outcomes discovered that those carrageenans can shape strong compacts with an excessive elastic recovery. The findings in the long run brought about the belief that the carrageenan's below research was made properly [81].

Soy polysaccharide

It is an herbal super disintegrant that can be utilized in nutritious items as it doesn't consist of any starch or sugar. A form of high molecular weight polymer called soy polysaccharide, obtained from soybeans, was evaluated as a disintegrant in tablets made using direct compression with lactose and dicalcium phosphate dihydrate as fillers. Cross-connected sodium carboxymethyl cellulose and corn starch were employed as a control. Soy polysaccharide performs wonderfully as a disintegrating agent in direct compression formulations, producing outcomes comparable to those of cross-connected CMC [82, 83].

Aegle marmelos gum

It is crafted from *Aegle marmelos fruits*, which dissolve greater quickly and uniformly than croscarmellose sodium. The mature fruit's scarlet pulp has a mucilaginous, astringent flavor. It makes medicines that are not very soluble greater soluble. It causes a significant shift in the liver, kidney, stomach, and intestine's GSH (glutathione) concentration. In diabetic people, it will also raise blood glucose levels and glycosylated hemoglobin. In diabetic individuals, it lowers plasma insulin and hepatic glycogen [84].

Alginates

An anionic polysaccharide, referred to as alginates or alginic acids, is a straight, unbranched polymer discovered in marine algae such as *Macrocystis pyrifera*, *Laminaria hyperborea*, and *brown seaweed* [85]. Seemed to be progressed through the alginate formula in a comparative study while as compared to the polylactide-coglycolide (PLG) formula. In the example of PLG, the nanoparticles had been created with the use of the emulsion-solvent-evaporation method, whilst, withinside the case of alginate, they had been created with the use of cation-brought on managed gelification [86].

Mangifera indica gum

Pandey and Nayak reported that "*Mangifera indica*, that's a member of the Anacardiaceous own circle of relatives and is frequently called mango, It is innocent and utilized in lots of formulations as a disintegrant, binder, postponing agent, and emulsifying agent. The gum powder has a coloration starting from white to off-white and is soluble in water; however nearly insoluble in acetone, chloroform, ether, methanol, and ethanol. Each and each part of the tree has pharmacological action, including diuretic, astringent, diabetic, asthma, diarrhea, urethritis, and scabies, and the gum is without problems available and toxic-free" [87, 88].

Plantago ovata seed mucilage

Singh and Ghenge reported that "The word "*psyllium*" or "*ispaghula*" is often used to consult some of *Plantago* species whose seeds are

used within the manufacture of mucilage. Plantago ovata's mucilage possesses lots of qualities, which include binding, dissolving, and assisting capabilities. In a study, various portions of Plantago ovata mucilage had been used as herbal super disintegrants to compress rapid dissolving drugs of amlodipine besylate. Weight variation, hardness, friability, disintegration time,

drug content, and solubility had been all assessed for every component. The progressed components demonstrate quicker *in vitro* dissolving within sixteen mins with a shorter *in vitro* disintegration time of 11.69 seconds. With a boom in herbal super disintegrant concentration, *in vitro*, disintegration time reduces" [89, 90].

Table 3: Summary of recent research on ODTs

Drugs	Excipient	Method	Outcome	Source
Efavirenz	Sodium starch glycolate, magnesium stearate	Direct compression (DC)	Faster drug release	119
Primaquine phosphate	B-cyclodextrin, lactose	DC	Reduce disintegration time	112
Lovastatin	Crospovidone, SSG	DC	Rapid onset of action and faster dissolution	110
Meclizine Hcl	tulsion 334, Explotab	DC	99.4% of the drug is released within 2 min	115
Cinnarizine	Indion 414, Polyplasdone xl	DC	High patient compliance	118
Diclofenac sodium	Crospovidone, Mannitol	DC	Better bioavailability and improved drug release	113
Quetiapine Fumarate	Magnesium stearate, Pearlitol SD-200	Sublimation	Less disintegration time and greater drug release	116
Levocetirizine dihydrochloride	Crospovidone, talc, Kyron T-134	DC	Within 10 min, 99.73% of the drug has been released.	111
Cyproheptadine HCl	Mannitol, Microcrystalline cellulose	DC	98.64% of the drug is released within 30 min	117
Triphala	Embellica officinalis	DC	Less dispersible time	114
Candesartan cilexetil	tulsion 339, magnesium stearate, Indion 204	DC	Good patient compliance	109

Future perspective of natural polymers

Oral administration is the most common and advised way of medication administration for both solid and liquid dosage types. Solid dosage forms are desirable due to the ease of administration, accurate dosing, self-medication, pain avoidance, and most importantly, patient compliance. Fast-dissolving tablets provide several significant advantages over conventional dosage forms, including improved efficacy, enhanced bioavailability, early onset of action, and greater patient compliance and acceptability. The usage of natural polymers, as opposed to synthetic polymers, has a considerable influence on the creation of fast-dissolving tablets. Oral administration is the preferred and most common way to provide medication for both solid and liquid dosage forms. Solid dosage forms are desirable due to their ease of administration, accuracy of dosage, ability to self-medicate, ability to reduce pain, and—most importantly—patient compliance. Fast-dissolving tablets provide several significant advantages over conventional dosage forms, including improved efficacy, enhanced bioavailability, early onset of action, and greater patient compliance and acceptability. Natural polymers are used instead of synthetic ones, which has a big influence on how fast-dissolving tablets are designed. Natural polymers increased the pace at which the drug was released from the tablet while reducing the time required for dissolving and disintegrating. Natural polymers are preferred over synthetic ones because they are non-toxic, freely available, inexpensive, utilized in small doses, and extracted naturally. Higher bioavailability and speedier pharmaceutical solubility provided by natural polymers result in more effective therapy and improved patient compliance.

Natural polymers have a more significant influence on fast-dissolving tablets than synthetic polymers do. Due to their improved rate of medicine release from the tablet and shorter dissolving and disintegration periods, natural polymers are utilized as binder super disintegrants and diluents. Since they may be naturally extracted to provide dietary supplements, natural polymers are preferred to synthetic ones because they are non-toxic, easy to get, affordable, and utilized in small doses. Natural super disintegrants offer more effective therapy and greater patient compliance due to their enhanced bioavailability and speedier pharmaceutical disintegration. Hence, natural polymers can be employed as disintegrants in tablet formulations.

CONCLUSION

Comparing orodispersible drugs to conventional stable dose bureaucracy can be advantageous. Of all of the new drug-transport methods, this one is one of the nice innovations. They provide better bioavailability, affected person compliance, convenience, and a brief

starting of action. ODTs can degrade in damp conditions; consequently, there's constantly a hazard that the synthetic drugs will deteriorate. Therefore, the packaging of the formulation must be cautiously studied. Additionally, it is n't a very good concept to fabricate medicines that want sustained launch as ODTs. Over the beyond ten years, ODTs have grown to be a lot greater broadly used. According to the literature review, it's miles viable to attract the realization that juvenile, geriatric, bedridden, and psychotic sufferers who be afflicted by dysphagia advantage maximum from orodispersible tablets. The availability of orodispersible tablets as over-the-counter medicines for the remedy of allergy, cold, and flu signs and symptoms has elevated recently. Polymers are critical for the transport of drugs. Consequently, deciding on the proper polymer is vital with inside the manufacturing of pharmaceuticals. Synthetic polymers do now no longer have the equal foremost effect on fast-dissolving drugs as herbal polymers do. Natural polymers are used as binder super disintegrants and diluents due to the fact they elevated the medicine launch price from the pill and reduced the dissolving and disintegration times. The utilization of numerous herbal polymers that may be hired withinside the components of orodispersible drugs has been emphasized withinside the present-day review.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All authors have contributed equally.

CONFLICT OF INTERESTS

All authors declare no conflict of interest

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