

Comprehensive Review on Fast Dissolving Tablets Using Natural and Synthetic Super Disintegrants

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ABSTRACT: The development of different formulations with improved performance and acceptability has resulted from the desire for improved attractiveness in oral administration. The demand for Fast Dissolving Tablets [FDTs] has increased over the past few decades as they have become an urgent trend in Novel Drug Delivery Systems [NDDS]. Dysphagia is a problem that can be encountered when taking medication through oral route. This condition is prevalent in patients who are either paediatric, geriatric, have neurological issues, or are bedridden. FDTs would be a superior option to tackle such a problem, as they will dissolve within seconds when touched with saliva and to provide quick medication absorption, reduced toxicity, and higher drug bioavailability.

Natural and synthetic superdisintegrants and other excipients are necessary for making this type of dosage form. In solid dosage form, superdisintegrants are usually used at a low level, typically with a weight of 1-10% of the total dosage. The demand for natural superdisintegrants has been high in recent times compared to synthetic or semi-synthetic ones. Their non-irritating and non-toxic properties, as well as their abundant availability, lower prices are the reasons for their popularity. diverse varieties of super disintegrants that are being utilized in formulation to offer safer and more effective drug delivery.

Keywords: Fast Dissolving Tablets, Natural superdisintegrants, synthetic superdisintegrants, Direct compression Fenugreek, Cross povidone.

I. INTRODUCTION

The oral administration route is both the most preferred and convenient for administration, which offers advantages such as ease of administration, high versatility, and patient compliance [1]. The most common solid dosage forms are tablets and capsules, but some patients may encounter significant drawbacks, the accessibility of readily available water can help overcome swallowing difficulties [2]. Dysphagia which means difficulty in swallowing is a common

problem for individuals of all age groups, particularly elderly and paediatric patients, because of physiological changes [3]. A key Novel Drug Delivery System [NDDS] that aims to enhance drug molecules safety and efficacy is Fast Dissolving Tablets [FDTs], which is rapidly becoming accepted, improving patient compliance by creating a convenient dosage form for administration [4]. FDTs provide a faster rate of dissolution, more absorption in the stomach, a simpler time swallowing, less first-pass metabolism, and an increased oral bioavailability. prompt response and increased adherence from patients.

The properties of FDTs are extraordinary for disintegration and can disintegrate quickly without having any water in your mouth in a few seconds, the rapid disintegration is caused by saliva quickly entering the pores of an FDT implanted within the mouth [5]. Super disintegrants are typically added to drug formulations to facilitate the breaking down the contents of tablets or capsules into smaller pieces, which dissolve more quickly than medications that don't disintegrate. The study proposes the use of direct compression method for formulating oral medication administration using FDTs, incorporating synthetic super disintegrants such as, calcium silicate, cross povidone, croscarmellose sodium, Croslinked Alginic acid and natural super disintegrants like, Fenugreek seed mucilage, Aegle marmelos fruit, locust bean, Mango peel pectin, Lepidium sativum mucilage, Plantago seed mucilage, Aegle marmelos gum, Hibiscus rosasinensis, Chitosan, Dehydrated banana powder [6]. In this study, we extracted fenugreek gum and evaluated its powder flow properties (bulk density, angle of repose, Carr's index and hausner ratio, tapped density), in order to determine fenugreek seed mucilage extract's disintegration efficiency against synthetic super disintegrant i.e. cross povidone in FDTs formulation. Measurement of the swelling index and loss on drying was conducted to evaluate the efficiency of super disintegrants at the optimal

concentration level. And the tablets were evaluated through a series of physical tests. [7]

Superdisintegrants:

Substances that achieve disintegration faster than conventionally used substances are known as superdisintegrants. The disintegration process of tablet capsule content leads to the formation of smaller particles that dissolve more rapidly than without disintegrants [8].

Criteria for selection of superdisintegrants:[9]

In selecting Superdisintegrants, many factors are taken into account.

1. The quantity of disintegrated materials presents in the preparing process.
2. Hardness of tablet.
3. Good flow properties.

4. Nature of drug.
5. A process that involves adding and mixing.
6. The presence of surface-active substances.
7. Less friable tablets can be formulated by compacting them.
8. It is beneficial for the patient to have a good mouth.

Classification of superdisintegrants:

Superdisintegrants can be categorized by their source of origin, as depicted in the figure1 [10, 11]

Co-processed superdisintegrants

The properties of co-processed excipients are better than those of individual excipients mixed in a physical mixture. Here are some examples of commercial excipients given in table1

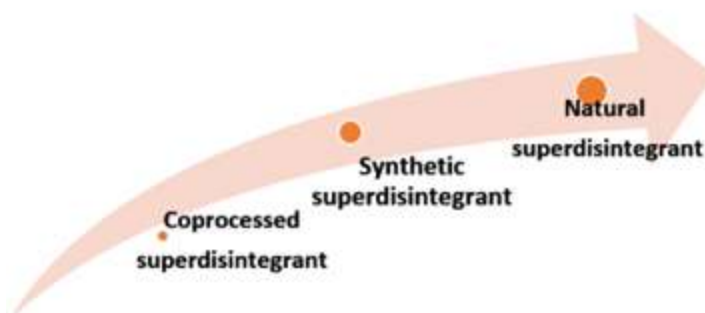


Figure1: Types of superdisintegrants.

Table1:List of co-processed superdisintegrants

Name of the co-processed superdisintegrants	Consists of
Ludipress	Lactose monohydrate, polyvinyl pyrrolidone, and crospovidone
Starlac	Lactose and maize starch
Starcap 1500	Corn starch and pregelatinized starch
Ran-Explo-C	Microcrystalline cellulose, silica, and crospovidone
Ran-Explo-S	Microcrystalline cellulose, silica, and sodium starch glycolate
Pan Excea MH300G	Microcrystalline cellulose, hydroxyl-propyl-methyl cellulose, and crospovidone
Ludiflast	Mannitol, crospovidone, and polyvinyl acetate

Synthetic super disintegrants

In order to speed up the disintegration of tablets, these synthetic superdisintegrants are

frequently used in formulation of a tablet. Table 2 provides instances of artificial superdisintegrants.

Table2: Synthetic superdisintegrants listed, and including information about their source and mode of action.

Name of the synthetic superdisintegrant	Nature	Brand available	Mechanism	Properties
Sodium starch glycolate/ sodium carboxymethyl starch	Modified starch/ cross-linked starch	Explotab Primogel Tablo Vivastar	Absorb water quickly results in swelling, swells 712 folds in less than 30 seconds	Swells in 3-dimension and high- level acts as a sustained release matrix
Crospovidone	Crosslinked PVP	M kollidon polypiasdone	Combination of swelling and wicking	Water-insoluble, spongy in nature
Croscarmellose sodium	Modified cellulose	Ac-Di-Sol Nymce ZSX primellose solutab vivasol L-HPC	Swelling and wicking within 10 seconds, swells up to 4-8 folds	Swells in 2-dimension
Croslinked alginic acid	-	Alginic acid NF	Rapid swelling or wicking	Promotes disintegration in both dry and wet granulation
Calcium silicate	-	-	Wicking action	Highly porous and have lightweight
Ion exchange resins	Crosslinked polyacrylic	Indion 414 Tulsion 339 Amberlite IRP 88	Swelling	Has high water uptake capacity and high purity pharmaceutical grade weak acid cation resin supplied in dry form

Natural superdisintegrants:

Numerous plant-based pharmaceutical excipients are available today, and multiple studies have looked into the potential applications of most of these plant-based substances as pharmaceutical superdisintegrants [12]. Many naturally occurring substances, such as gums, mucilage, as well as other materials obtained from natural resources, are included in the category of natural superdisintegrants. karaya gum, and agar have all been used to define mouth-dissolving tablets. Natural resources that have established themselves in the pharmaceutical sector are the source of gums

and mucilage. These work best as thickening, emulsifying, stabilizing, granulating, gelling, binding, suspending, and super disintegrating agents during the film-forming process.

As new news sources are developed and located, the importance of these normal root assets is gradually increasing. The preference for regular super crumbles over manufactured as well as semi-engineered disintegrants stems from their inferior quality, effective accessibility, non-aggravation nature. They have soothing activities in addition to environmentally friendly surroundings. Eco-friendly super disintegrants [13].

Table3: Fast-dissolving tablets contain natural polymers.

S. no.	Natural polymer	Marketed drug	Disintegration time	Concentration used
1	Chitin and chitosan	Cinnarizine	60 sec	3% w/w
2	Guar gum	Glipizide	30 sec	1% w/w
3	Gum karaya	Amlodipine, granisetron hydrochloride	17.10 sec	4% w/w
4	Agar and treated agar	Theophylline	20 sec	1-2% w/w
5	Fenugreek seed mucilage	Metformin hydrochloride	15.6 sec	4% w/w
6	Soy polysaccharide	Lornoxicam	12 sec	8% w/w
7	Gellan gum	Metronidazole	155 sec	4% w/w
8	Mango peel pectin	Aceclofenac	11.59 sec	0.1-4% w/w
9	Lepidium sativum mucilage	Nimesulide	17 sec	5-15% w/w
10	Plantago ovata seed	Granisetron HCl	17.10 sec	5% w/w

	mucilage			
11	Aegle marmelos gum	Aceclofenac	8–18 min	6% w/w
12	Locust bean gum	Nimesulide	13 sec	10% w/w
13	Lepidium sativum	Nimesulide	17 sec	10% w/w
14	Mangifera indica gum	Metformin HCL, paracetamol	3–8 min	6% w/w
15	Hibiscus rosa-sinensis mucilage	Aceclofenac	20 sec	6% w/w
16	Dehydrated banana powder	Ondansetron HCl/propranolol, gabapentin	15–36 sec	6% w/w

Mechanism of Action of Superdisintegrant:[15]



Figure:1 Mechanism of action of superdisintegrant

Preformulation Configurations:

Characterization of Synthetic and Natural Superdisintegrants. Physico-chemically

Swelling index: A 100 ml stoppered graduated cylinder was used for the study. One gram of powder's initial bulk volume was recorded. After an hour of vigorous shaking every ten minutes, enough water was added to ensure 25 milliliters of uniform dispersion, and the mixture was left to stand for twenty-four hours. After a day, the sediment volume of the swollen mass was measured while the dispersion was kept at room temperature.

$$\text{Index of swelling} = 100 \times (V2 - V1 / V1)$$

Where V2 is the volume of the hydrated material and V1 is the initial volume of the material prior to hydration.

Loss on Drying: This method is employed to ascertain whether a sample contains high concentrations of moisture or solvents. After being weighed (W1), the material sample was heated for two hours in an oven. After cooling in the desiccator's dry atmosphere, it was weighed in the end (W2).

$$\% \text{ loss on drying} = [(W1 - W2) / W1] \times 100, \text{ where } W1 \text{ and } W2 \text{ are the powder's starting and final weights, respectively.}$$

pH: A digital pH meter was used to measure the pH of one gram of powder suspended in 100 milliliters of distilled water.

Solubility: A powder sample is dissolved in aqueous, organic, and inorganic solvents to ascertain its solubility.[16]

Fenugreek

The dicotyledon leguminous annual fenugreek (*Trigonella foenum-graecum* L.) is widely used as a herb and spice. Although it originated in an area that stretched from Iran to Northern India, it is currently grown in China, North and East Africa, Greece, and Ukraine. Among them is fenugreek. the oldest known medicinal plants; for this reason, it is referred to as "an old world" crop for the "new world." Its oil component and alkaloids, which are nontoxic when consumed, give it a bitter taste; defatted fenugreek seeds don't taste bitter. The morphology, growth habit, biomass, and capacity for seed production of different fenugreek genotypes vary. Three highly significant components of significant medicinal importance are found in the seed and to a lesser extent in the leaves: complex carbohydrates seeds don't taste bitter. The morphology, growth habit, biomass, and capacity for seed production of different fenugreek genotypes

vary. Three highly significant components of significant medicinal importance are found in the



Figure:2 Leaves of *T. feonumgraecum*



seed and to a lesser extent in the leaves

Fenugreek's nutritional and medicinal constituents

Fenugreek is a special kind of useful food crop [17]. Both the seed and the leaves are valuable for food and medicine because of their chemical composition. Besides providing a wealth of macro- and micronutrients, they also deliver a variety of phytochemicals, which are non-nutritive plant chemicals with disease-preventive or protective qualities. These phytochemicals also give the leaves their well-known spicy flavor. Organoleptic properties and nutritious contents are two categories that can be used to group various aspects of nutritional value. Famous and well-liked for their potent, spicy flavor and high fiber content are fenugreek seeds [18]. Fenugreek leaves, when dried, are used to enhance the flavor of meat, fish, and vegetable preparations. The primary compound that gives fenugreek its unique sweet scent is sotolon. There are trace amounts of both volatile and fixed oils in fenugreek seed. [19]

Fenugreek's Pharmacoeutical Benefits

Natural resources have provided therapeutic treatments for millennia, and 80 percent of the world's developing and developed nations still rely heavily on plant-based primary healthcare systems. [6] Ayurveda claims that plants contain a wide variety of constituents that can be used to treat a wide range of illnesses. Herbal medications have fewer adverse effects and are more readily available. These days, there is a huge global attraction to herbal plant medications. Fenugreek is widely accessible in our kitchen and has long been used as a medication. Fenugreek was traditionally used to facilitate childbirth and increase milk flow. It is still used traditionally to treat a variety of illnesses; for

example, Egyptian women take it for menstrual pain, and tourists drink it as hilba tea to ease stomach issues; fresh fenugreek leaves are used to treat indigestion, flatulence, and a sluggish liver [20]

Traditionally used as a herb, fenugreek is incredibly rich in phytochemicals like alkaloids, steroids, and flavonoids that have been recognized and segregated by pharmaceutical firms or industries involved in the production of medicinal and hormonal drugs. One of the more traditional medicinal applications of fenugreek seeds is the treatment of eczema or other inflammatory conditions; this practice is still carried out today in many nations. Approximately 6-8% of the weight of the seeds is made up of the fenugreek extract. It was also applied as a tonic and remedy for leg edema and weakness [21]

Activity of Antioxidants

It has been studied whether the flavonoids in fenugreek extract have antioxidant properties. In a recent study. It has been reported that fenugreek seed extract stops hemolysis and lipid peroxidation in red blood cells. It has also been demonstrated that fenugreek seeds increase antioxidant levels and lower liver peroxidation in the livers of diabetic rats. In the mitochondria of rat liver cells, the seed extract demonstrated hydroxyl radical scavenging and hydrogen peroxide-induced LPO inhibition. The deoxyribose system and pulse radiolysis were used to show the extract's ability to scavenge OH. The extract from fenugreek seeds has antioxidants that guard against oxidative damage to cellular structures. The antiradical and in vitro antioxidant properties of an aqueous methanolic extract of fenugreek were studied in a number of model systems. [22]

Impact of Enzymatic Processes

Numerous studies have demonstrated that fenugreek can partially restore the functions of important enzymes, specifically those that deal with lipids and carbohydrates, in both human and animal models. Trigonella treatment reduced hyperglycemia and restored the altered enzyme activities in rats. The combined dose of insulin, vanadate, and fenugreek was used to treat the

lowered levels of superoxide dismutase, glutathione peroxidase, and antioxidant enzymes catalase in the liver and kidney of experimental diabetic rats. This study found that fenugreek seed extract⁴⁴ reduces the activities of glucose 6-phosphatase and fructose-1, 6-biphosphatase in the liver and kidneys of diabetic rats.[23]

Synthetic superdisintegrants

Table 4: list of superdisintegrant and their mechanism

S. No.	superdisintegrant name	Nature	Brands available	Mechanism	Properties
1	Sodium starch Glycolate/sodium carboxymethyl starch	Modified starch /Cross-linked starch	Explotab Primogel Tablo Vivastar	Absorb water quickly results in swelling, swells 7-12 folds in less than 30 seconds	Swells in 3 dimension and high level acts as sustained release matrix
2	Crospovidone	Cross-linked PVP	M Kollidon Polypladone	Combination of swelling and wicking	Water insoluble, spongy in nature
3.	Croscarmellose Sodium	Modified cellulose	Ac-Di-Sol Nymce ZSX Primellose Solutab Vivasol L-HPC	Swelling and wicking within 10 seconds, swells upto 4-8 folds	Swells in 2 dimension
4	Croslinked Alginic acid	-	Alginic acid NF	Rapid swelling or wicking	Promotes disintegration in both dry and wet granulation
5.	Calcium silicate	-	-	Wicking action	Highly porous and have light weight
6.	MCC and L-HPC				
7.	Ion exchange resins	Crosslinked polyacrylic	Indion 414 Tulsion 339 Amberlite IRP 88	Swelling	Has high water uptake capacity and high purity pharmaceutical grade weak acid cation resin supplied in dry form.
8	Chitin and Chitosan	-	-	Swelling	-

Cross-linked polyvinylpyrrolidone (crospovidone)

Crospovidone quickly wicks saliva into the tablet to generate the volume expansion and hydrostatic pressures necessary to provide rapid disintegration in the mouth. Unlike other superdisintegrants, which rely principally on swelling for disintegration, Crospovidone superdisintegrants use a combination of swelling and wicking. When examined under a scanning electron microscope, crospovidone particles appear granular and highly porous. This unique, porous particle morphology facilitates wicking of liquid into the tablet and particles to generate rapid disintegration. Due to its high crosslink density, crospovidone swells rapidly in water without gelling. Other superdisintegrants have a lower crosslink density and, as a result, form gels when fully hydrated, particularly at the higher

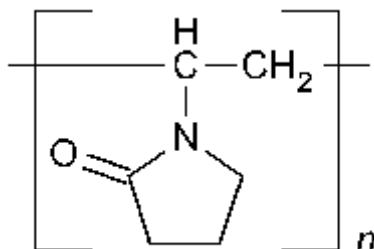
use levels in ODT formulations. Unlike other superdisintegrants which are either poorly compressible or non-compressible, Crospovidone disintegrants are highly compressible materials as a result of their unique particle morphology. In contrast to sodium starch glycolate and croscarmellose sodium, Crospovidone superdisintegrants exhibit virtually no tendency toward gel formation, even at high use levels. Disintegrants that gel can result in ODT and chewable products with an unpleasant, gummy texture.

Properties of cross povidone

Name of the excipient : Cross povidone

IUPAC Name: 1-ethenylpyrrolidin-2-one

Chemical Structure : Poly vinyl polypyrrolidone



Molecular Formula : (C₆H₉NO)_n

Molecular weight : (111)_n

Category : Super Disintegrate

The pharmaceutical industry has extensively documented the use of crospovidone, an insoluble form of polyvinylpyrrolidone, as a tablet excipient, which functions as a tablet disintegrant and binder. In medicine, it is used as a germicide to treat wounds and as a solubilizing excipient to increase the bioavailability of medications (like steroids) for the treatment of various intestinal disorders. It is also frequently added to alcoholic and non-alcoholic beverages as a clarifier. This chapter covers the preparation techniques for crospovidone as well as its physical characteristics and main applications. Although it can also be used as a tablet binder, the main pharmaceutical use for crospovidone is as a tablet disintegrant. In order for a polymer to find application as a pharmaceutical excipient, certain material grades must meet certain requirements.

Evaluation of Fast Dissolving Tablets

All formulations' FDTs underwent Quality Control testing, and the average values were computed. A variety of parameters, including appearance, weight variation, hardness, thickness, friability, wetting time, water absorption ratio, disintegration time, and in vitro dissolution study, were assessed for each tablet.

Appearance

From every formulation were chosen at random, and organoleptic characteristics like colour, flavour, and shape Pills were assessed.

Weight variation

From each batch, twenty tablets were chosen at random and weighed separately on an electronic balance (Shimadzu). The weight variation is then compared between the weighed individual and the average weight.

Hardness

The Monsanto hardness tester was used to measure the tablet hardness for each formulation.

Wetting Time

A double-folded piece of tissue paper (10.75 x 12 mm) was put in a culture dish (d = 6.5 cm) with 6 ml of water. The amount of time it took for a tablet to completely wet the paper was measured.

Water Absorption Ratio

The test was conducted using the same methodology as the wetting time. In this test, the tablet was first weighed before being placed on a petridish.

Following thorough wetting, the tablet was removed and weighed. Ratio of water absorption, or R, was calculated using the formula

$$R = 100(W_b - W_a) / W_a$$

Where W_a is the tablet's weight prior to water absorption

W_b is the tablet's weight following absorption.

Disintegration Time

The same methodology used for the wetting time was applied to the test. The tablet was weighed for this test before it was put on a petridish.

The tablet was taken out and weighed after it had been thoroughly wetted. R = 100(W_b - W_a) / W_a is the formula used to calculate the ratio of water absorption, or R.

Where W_a is the weight of the tablet before it absorbs water.

W_b is the weight of the tablet after it has been absorbed.

II. CONCLUSION

The rapidly disintegrating drug delivery systems have emerged as a significant area of

current research due to the growing need for innovative drug delivery methods. Superdisintegrants Reduce the disintegration time and increase the drug release rate from the tablets. The use of natural superdisintegrants for the quick disintegration of tablet structure is always a topic of active research, despite the availability of a wide range of materials to serve as superdisintegrants in the design of dispersible tablets. Natural superdisintegrants are becoming more and more appealing because they are easily found in nature, reasonably priced, derived from living things, easily degrade in vivo, non-toxic, and amenable to chemical changes. In the pharmaceutical sector, they play crucial role Consequently, in order to have better materials for pharmaceutical applications, there will be ongoing interest in natural superdisintegrants in the years to come.

REFERENCES

- [1]. Bhowmik, D., Chiranjib, B., & Chandira, R. M. (2009). Fast dissolving tablet: an overview. *J Chem Pharm Res*, 1(1), 163–177.
- [2]. Konapure, S. A., Chaudhari, P. S., Oswal, R. J., Kshirsagar, S. S., Antre, R. V., & Chorage, T. V. (2011). Mouth dissolving tablets” an innovative technology. *Int J Appl Biol Pharm Technol*, 2(1), 496–503.
- [3]. Karthikeyan, M., Umarul, M. A. K., Megha, M., & Shadeer, H. P. (2012). Formulation of Diclofenac tablets for rapid pain relief. *Asian Pacific Journal of Tropical Biomedicine*, 2(1), S308–S311. [https://doi.org/10.1016/s2221-1691\(12\)60179-8](https://doi.org/10.1016/s2221-1691(12)60179-8)
- [4]. Kumar, S., Gupta, S. K., & Sharma, P. K. (2012). A review on recent trends in oral drug delivery-fast dissolving formulation technology. *Adv Biol Res*, 6(1), 6–13.
- [5]. Puttewar, T. Y., Kshirsagar, M. D., Chandewar, A. V., & Chikhale, R. V. (2010). Formulation and evaluation of orodispersible tablet of taste masked doxylamine succinate using ion exchange resin. *Journal of King Saud University. Science*, 22(4), 229–240. <https://doi.org/10.1016/j.jksus.2010.05.003>
- [6]. Sona, P. S., & Muthulingam, C. (2011). Formulation and evaluation of taste masked orally disintegrating tablets of diclofenac sodium. *Int J PharmTech Res*, 3(2), 819–826.
- [7]. Ravi S, Teja KM, Sai KV, Scholars Academic Journal of Pharmacy, 2013, 2, 4, 340-353.
- [8]. Neeti Anand, Singh, L., Sharma, V., & Tablets, E. O. N. S.-D. I. O.-D. (n.d.). Vijay Sharma. AN OVERVIEW; INTERNATIONAL RESEARCH RESEARCH OF PHARMACY, 2013(8).
- [9]. Verma, J., Prajapati, D. S., & Irchhiaya, A. N. (2017). AN OVERVIEW ON SUPERDISINTEGRANTS: A REVIEW. *EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH*, 4(09), 252–260.
- [10]. Shihora, H., & Panda, S. (2011). Superdisintegrants, utility in dosage forms: a quick review. *J Pharm Sci*, 1(3), 148–153.
- [11]. Mohanachandran, P. S., Sindhumo, P. G., & Kiran, T. S. (2011). Superdisintegrants: an overview. *Int J Pharm Sci Rev Res*, 6(1), 105–109.
- [12]. Beneke, C., Viljoen, A., & Hamman, J. (2009). Polymeric plant-derived excipients in drug delivery. *Molecules (Basel, Switzerland)*, 14(7), 2602–2620. <https://doi.org/10.3390/molecules14072602>
- [13]. Pokhariya, P., Ganarajan, G., & Kothiyal, P. (2016). Formulation and evaluation of mouth dissolving tablet of telmisartan using natural superdisintegrants. *Indo Am J Pharm*, 3(7), 713–727.
- [14]. Basch, E., Ulbricht, C., Kuo, G., Szapary, P., & Smith, M. (2003). Therapeutic applications of fenugreek. *Alternative Medicine Review: A Journal of Clinical Therapeutic*, 8(1), 20–27.
- [15]. Duppala, L., Girinath, K. S., & Kumar, D. M. (2016). Fast dissolving dosage forms: an overview. *World Journal of Pharmaceutical Research*, 5(10), 1184–1200.
- [16]. Fotopoulos, C. (2002). Fenugreek - The genus *Trigonella*, New York (G. A. Petropoulos, Ed.). Taylor and Francis.
- [17]. Kakani, R. K., Anwer, M. M., Meena, S. S., & Saxena, S. N. (2009). Advance production technology of fenugreek. *NRCSS Tech. Release*, 1–24.
- [18]. Kaviarasan, S., Naik, G. H., Gangabhairathi, R., Anuradha, C. V., & Priyadarsini, K. I. (2007). Antiradical and Antioxidant Activity, *Food Chemistry*. 103. 31–37.

- [19]. King, A., & Herman, W. H. (1998). Global burden of diabetes, 1995- 2025: prevalence, numerical estimates, and projections. *Diabetes Care*. 21, 1414–1431.
- [20]. Meghwal, M. (2012). A review on the functional properties, nutritional content, medicinal utilization and potential application of fenugreek. *Journal of Food Processing & Technology*, 03(09). <https://doi.org/10.4172/2157-7110.1000181>
- [21]. Najma, Z. B., Pardeep K Asia T Kale, R. K., Cowsik, S. M., & Mclean, P. (n.d.). Metabolic and molecular action of *Trigonella foenum-graecum*.
- [22]. Sowmya, P., & Rajyalakshmi, P. (1999). Hypocholesterolemic effect of germinated fenugreek seeds in human subjects. *Plant Foods for Human Nutrition (Dordrecht, Netherlands)*, 53(4), 359–365.
- [23]. Uday, K. M., & Kishore, B. M. (2014). Design and evaluation of fast dissolving tablets containing diclofenac sodium using fenugreek gum as a natural superdisintegrant. *Asian Pacific J of Tropical Biomedicines*, 4(1), 329–334.
- [24]. Najma, Z. B., Pardeep K Asia T Kale, R. K., Cowsik, S. M., & Mclean, P. (n.d.). Metabolic and molecular action of *Trigonella foenum-graecum*.
- [25]. Sowmya, P., & Rajyalakshmi, P. (1999). Hypocholesterolemic effect of germinated fenugreek seeds in human subjects. *Plant Foods for Human Nutrition (Dordrecht, Netherlands)*, 53(4), 359–365.
- [26]. Uday, K. M., & Kishore, B. M. (2014). Design and evaluation of fast dissolving tablets containing diclofenac sodium using fenugreek gum as a natural superdisintegrant. *Asian Pacific J of Tropical Biomedicines*, 4(1), 329–334.
- [27]. Vrudnic, E. M., Lausier, J. M., Chilamkarti, R. N., & Rhodes, C. T. (1980). Studies on the utility of cross-linked polyvinylpyrrolidone as a tablet disintegrant. *Ind. Ind. Pharm*, 6, 291–309.
- [28]. Banker, G. S. (1970). The theory and practice of industrial pharmacy. *Journal of Pharmaceutical Sciences*, 59(10), 1531. <https://doi.org/10.1002/jps.2600591046>