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To Formulation and Evaluation Fast dissolving tablet of Glipizide.

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ABSTRACT :

Aim of the present study was to develop the Fast-Dissolving Oral flicks of Glipizide. It's alternate- generation sulfonylurea that can acutely lower the blood glucose position. Fast dissolving oral flicks deliver medicine directly in the vascular system and bypasses the hepatic first pass metabolism so cure of the medicine may also reduce significantly. Fast dissolving flicks were prepared using solvent casting system, hydrophilic polymers (HPMC K- 15, HPMCE-15, HPMC K- 100) were named as film forming agents and cut- 400 was used as plasticizer to give inflexibility to the flicks. In FT- IR study no commerce was observed between medicine and the excipients. Three blank flicks were named for the objectification of medicine. After characterization the medicine loaded flicks and studying their decomposition time & in- vitr medicine release studies, among them was named the stylish expression as its decomposition and dissolution time was less and it releases medicine to a lesser extent from 93 to further than 100 in ten twinkles. expression was named stylish expression as its decomposition and dissolution time was less and it released medicine to a lesser extent compared to other phrasings. thus, presto dissolving oral flicks can play an important part in oral medicine delivery. Drug loaded flicks with both the polymers were stable under 40 °C/ 75 RH conditions.

Keywords: Fast Dissolving Tablets, Glipizide, HPMC, Solvent casting method, Drug release.

INTRODUCTION

Fast Dissolving Tablets (FDTs)

Fast dissolving tablets, in general, are defined as solid oral lozenge forms that disintegrate and dissolve in mouth without water within 60 seconds or lower (Pfister and Gosh, 2005). According to fda's center for medicine evaluation and exploration (cder), fast dissolving tablets are defined as" a solid lozenge form containing medicinal substances, which disintegrates fleetly generally within a matter of seconds, when placed on the lingo"(fda-guidance for assiduity, 2007). The growing significance of fast dissolving lozenge forms is honored by assiduity as well as academia. The global trade for fast dissolving tablets was estimated at$ 2.4 billion in 2004 and$ 3 billion in 2006 (van arnum, 2006). Grounded on different technologies more than 50 marketable products are available in the request. These products can deliver medicines like desloratadine (antihistamine), piroxicam (nsaid), risperidone (antipsychotic), rizatriptan (antimigraine), famotidine(anti-ulcer), ondansetron (antiemetic), selegiline (antiparkinson) and roxithromycin (antibiotic). This growing significance was underscored lately when european pharmacopoeia espoused the term orodispersible tablet and before this time fda, issued draft guidance, guidance for assiduity orally disintegrating tablets. According to european pharmacopoeia, orodispersible tablet is" a tablet which disperses and disintegrates in lower than 3 twinkles in the mouth before swallowing". The draft guidance issue lately by the fda recommended, in addition to the original description, orally disintegrating tablets be considered solid oral medications that disintegrate fleetly in the oral depression with an in vitro decomposition time of roughly 30 seconds or lower, when grounded on the united states pharmacopoeia decomposition test system or volition (fda- guidance for assiduity, 2007). Fdts release medicine in the mouth for immersion through original oromucosal apkins and through pregastric (eg. Oral depression, pharynx, and esophagus), gastric (i.E.Stomach), and postgastric (eg.Small and large bowel) parts of the gastrointestinal tract (pfister and gosh, 2005).

Advantages of Fast Dissolving Tablets

The benefits of fast dissolving tablets are outlined below.
ease of administration to pediatric, senior and psychiatric cases. Accessible administration to cases who cannot swallow, similar as the mentally ill, impaired and uncooperative, stroke victims, healthcare facilities and bedridden cases.

1. It enables effortless termination of solution.
2. It provides quick dissolution of the medicine and immersion, which may result in a rapid onset of action. Certain medications can be absorbed from the mouth, throat, and esophagus as the medication travels through the stomach. This pregastric immersion may give bettered bioavailability. Pregastric immersion can potentially decrease the effectiveness of the medicine if a substantial amount of it is metabolized in the liver. Due to the decrease in lozenge, it may lead to improved clinical performance and a decrease in unwanted side effects.

3. It possesses all the benefits of solid lozenge forms, such as enhanced stability, precise dosing, effortless manufacturing, compact packaging, and hassle-free case management.
4. The main advantage of this lozenge form is that it is beneficial for those who are constantly on the move and do not have immediate access to water. It can be easily swallowed by busy individuals.
5. These lozenge forms have the ability to provide the benefits of liquid medication in the form of solid medication. These benefits include simple administration and the absence of the risk of suffocation caused by physical inhibition from a lozenge form.
6. Fast dissolving tablets are classified as a novel lozenge form. Consequently, pharmaceutical companies may gain various benefits comparable to line extension and life cycle management, patent extension, exclusivity of product development, and product isolation..

Desirable characteristics and experimental challenges of FDTs.

The desirable characteristics of FDTs are described below

- rapid breakdown.
- Fruits and vegetables should be consumed without the need for additional water or with only a small amount of water. The decomposition fluid is provided by the slaver of the case. The broken tablet should be in a soft paste or liquid suspension, which can provide a pleasant mouthfeel and easy swallowing. The 'rapid decomposition' typically refers to the breakdown of tablets within a time frame of less than 1 nanosecond, although it is preferable to achieve decomposition as quickly as possible.
- Since fdts dissolve or disintegrate in the mouth, the medicine will not be completely dissolved in close proximity to the taste kids. After consuming food, there should be no leftover particles or residue in the mouth.
- For the optimal fdt technology, the medicine parcels should not significantly alter the tablet's properties. The presence of multiple medicine parcels has the potential to impact the functioning of fdts. For example, the solubility, shape, size, moisture absorption, compressibility, and flow properties of a medicine can greatly impact the final tablet's properties, just like the tablet's strength and decomposition.
- tablet strength and porosity
- Since fdts are engineered to dissolve rapidly, the tablet's porosity is typically maximized to ensure efficient water absorption. The essential components of the tablets are the rapid absorption of water into the tablets and the breakdown of associated patches into separate components for quick dissolution. This necessitates that excipients should possess high wettability, and the tablet structure should also exhibit a predominantly permeable network.
- Fdts should have low perceptivity to moisture. This issue can be particularly challenging because many water-soluble excipients are used in the formulation of oral dosage forms to enhance dissolution rates and provide a pleasant mouthfeel.

Materials And Methods

- Glipizide, Soluble starch, Talc, Magnesium stearate, Microcrystalline cellulose, Maize starch
- Preparation of Fast Dissolving Tablets
- Screened materials passed through a no. 100 screens were selected as superdisintegrants. Glipizide, microcrystalline cellulose, superdisintegrant and soluble starch were weighed and mixed together for 5 min in a resealable plastic bag. The powder blends were lubricated with talc and magnesium stearate to make flow property excellent. The powder blends ready for compression were transformed into tablets using a tablet punching machine (Cadmach, India) at a compression force of 3.5 tons.

Formulation composition of Glipizide

Table: Formulation composition of Glipizide

Ingredients (%)	**Formulation code**						
	TPOH 1	TPOH 2	TPOH 3	TPOH 4	TPOH 5	TPOH 6	TPOH 7
Glipizide	2	2	2	2	2	2	2
TPOH	1	3	5	7	9	12	15
MCC	35	35	35	35	35	35	35
Talc	1	1	1	1	1	1	1
Magnesium stearate	1	1	1	1	1	1	1
Starch soluble q.s. (mg)	250	250	250	250	250	250	250

Evaluation of Fast Dissolving Tablets

• pharmacological analysis.

An unidentified tablet was crushed in a glass mortar and pestle, and the powdered tablet was suspended in 100 ml of phosphate buffer (pH 7.4) using a glamorous stirrer. After 24 hours, the outcome was analyzed using a UV-1800 spectrophotometer (Shimadzu, Japan) at a wavelength of 225 nm. The medicine dosage was determined using the equation.

Drug content = [practical drug content/ theoretical drug content] ×100.

To ensure consistency in the assessment, a random selection of 10 tablets was labeled without any predetermined order and analyzed collectively using a uv-1800 spectrophotometer (shimadzu, japan) at 225 nm. The necessary requirement for this examination is that the consistency of the lozenge units should be within the range of 85 to 115, with a relative standard deviation not exceeding 6.

To assess the hardness of the tablets, 6 tablets were randomly selected from each batch. The hardness test was performed using a monsanto hardness tester (cadmach, ahmedabad, india). The friability test was performed using a roche friabilator (Campbell Electronics, Mumbai, India). A sample of 20 tablets was randomly selected from each batch and tested together. After completing 100 turns, the tablet samples were evaluated by weighing them.

The study on in vitro disintegration time for fast dissolving tablets was conducted using a modified disintegration test apparatus with distilled water, 0.1 m hcl, and phosphate buffer (ph 7.4) serving as the disintegrating medium (khan et al., 2007). A more appropriate device was created due to numerous studies (morita et al., 2000, watanabe et al., 2004, narazaki et al., 2004, watanabe et al., 2001) highlighting the inadequacy of the traditional disintegration test equipment for fast-dissolving tablets. In summary, the setup included a 1000 ml glass beaker with a wire basket held in place by a support, so that when the beaker held 900 ml of the disintegrating medium, the tablet in the basket was fully submerged. A small magnet was placed at the bottom of the beaker, which was being held at a temperature of 37 ± 20 degrees Celsius. The time it took for the material to break down was evaluated at a speed of 25 rpm.

• wetting time study

The wetting time of each tablet was examined in distilled water, 0.1 m hcl, and phosphate buffer (ph 7.4), following the method outlined by bi et al, with some modifications. A sheet of tissue paper folded twice was placed in a culture dish filled with 10 ml of distilled water, which also contained 0.1 m hcl and phosphate buffer at a pH of 7.4. A tablet containing a small quantity of amaranth powder was placed on top of the tissue paper. The time it took for the tablet's upper surface to turn red was recorded as the wetting time.

• comprehensive research.

The tablet's swelling was evaluated using various media, including distilled water, 0.1 m hcl, and phosphate buffer (ph 7.4). In the extensive study, the tablet's initial weight was recorded (w1). Subsequently, each tablet was individually placed in a 25-ml beaker filled with tissue paper soaked in swelling solution. After 2 minutes, the tablets were removed from the filter paper, cleaned, and re-measured (w2). The swelling index was calculated using the specified method.

Swelling index = [(w2–w1) / w1] 100.

• in vitro dissolution study

In the formulation, the evaluation of glipizide release was performed according to the guidelines provided in the usp monograph (usp, 2011). The test was conducted using paddles rotating at 50 rpm, and the dissolution medium was made up of 900ml of phosphate buffer at ph 7.4 and 0.1 m hcl kept at a temperature of 37°c. A volume of two milliliters of dissolution medium was taken at 0.25, 0.5, 0.75, 1, 1.5, 2, and 2.5 hours, filtered with a membrane filter, and examined using a uv-1800 spectrophotometer (shimadzu, japan). New form of communication was established after the removal of the sample. The commercially available formulation for the dissolution device and medium had a similar design to the fdts.

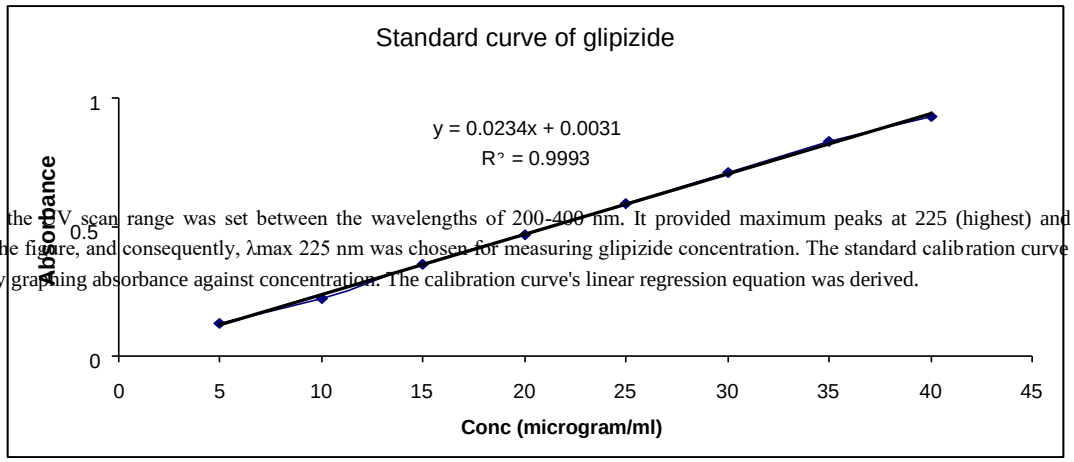
• differential scanning calorimetric (dsc) analysis

The dsc evaluation of pure glipizide and its physical mixture with excipient (1:1) was performed using dsc no 7 (perkin elmer) to assess any potential interactions between the drug and polymer. Samples were analyzed from 40 to 4000 c at a heating rate of 100 c min-1 while under a nitrogen purge with an approximate flow rate of 50 ml min-1. Samples (2-6 mg) were carefully measured and stored in standard aluminum containers, ensuring their safety and integrity.

Result and Discussion

Standard Calibration Curve of Glipizide

Fig: Absorption maxima of glipizide in phosphate buffer (pH 7.4)



To acquire λ, the UV scan range was set between the wavelengths of 200-400 nm. It provided maximum peaks at 225 (highest) and 276 nm, as illustrated in the figure, and consequently, λmax 225 nm was chosen for measuring glipizide concentration. The standard calibration curve for glipizide was created by graphing absorbance against concentration. The calibration curve's linear regression equation was derived.

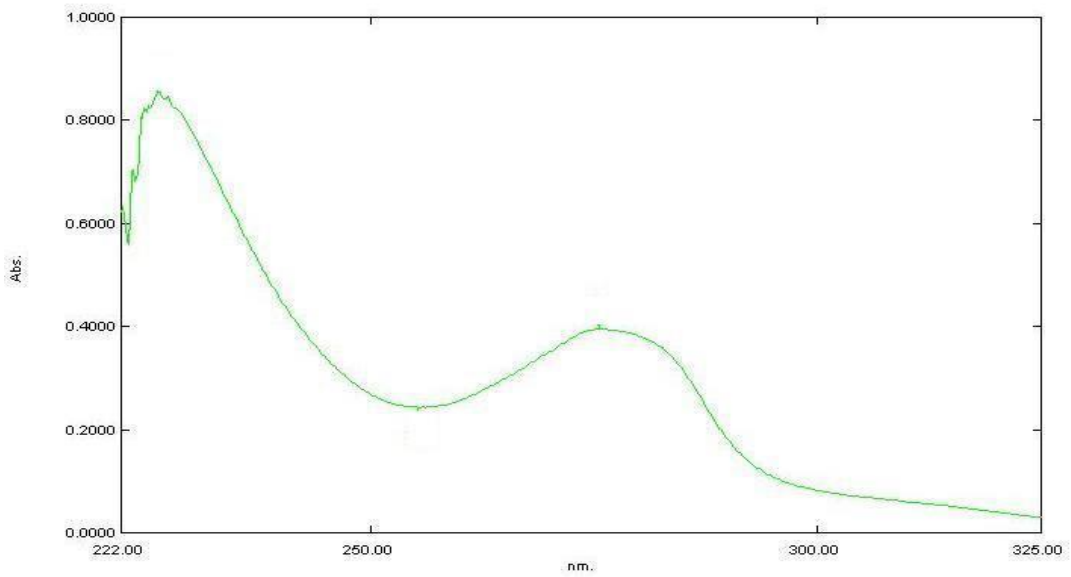


Fig: Standard curve of glipizide in phosphate buffer (pH 7.4) at λ 225 nm max

The hardness of the formulations varied from 4.06 ± 0.23 to 8.56 ± 0.25 Kg. The formulation with 1% of TPOH exhibited the highest hardness. Illustrated the impact of TPOH concentration on the hardness of the tablets. A negligible relationship ($p>0.05$), showing negative correlation ($R2=0.9812$), was observed between TPOH concentration and tablet hardness, suggesting that an increase in TPOH concentration led to a decrease in tablet hardness.

Table: Evaluation Table for Drug Content Analysis and Content Uniformity

Sr. no.	Formulation code	Drug content (%) (n=3, ± SD)	Content Uniformity (%) (n=10, ± SD)
1	TPOH1	100.62 ± 1.77	99.23 ± 1.83
2	TPOH2	99.19 ± 2.61	100.31 ± 1.93
3	TPOH3	99.87 ± 1.41	99.23 ± 2.23
4	TPOH4	99.62 ± 0.98	99.48 ± 1.22
5	TPOH5	99.33 ± 1.70	100.40 ± 1.57
6	TPOH6	100.31 ± 0.74	99.97 ± 1.58
7	TPOH7	100.13 ± 0.77	99.23 ± 1.32

Table: Evaluation Table for Hardness, Friability (%) and Disintegration Time

Sr. no.	Formulation code	Hardness (Kg) (n=6, ± SD)	Friability (%) (n=3, ± SD)	Disintegration time (sec) (n=3, ± SD)
1	TPOH1	8.56 ± 0.25	0	84.33 ± 4.35
2	TPOH2	8.33 ± 0.11	0.03 ± 0.03	75.99 ± 3.51
3	TPOH3	7.96 ± 0.25	0.04 ± 0.01	62.32 ± 3.78
4	TPOH4	6.56 ± 0.11	0.06 ± 0.01	56.66 ± 2.51

5	TPOH5	6.30 ± 0.43	0.14 ± 0.04	51.32 ± 2.08
6	TPOH6	5.66 ± 0.30	0.26 ± 0.03	44.33 ± 3.60
7	TPOH7	4.06 ± 0.23	0.31 ± 0.03	32.99 ± 2.51
		P>0.05, NS R^2= - 0.9812	P=0.008, S R^2= 0.9688	P=0.0001, HS R^2= - 0.9854

As the concentration of TPOH rose from 1 % to 15 % w/w, the percentage of friability grew from 0 % to 0.14 %. In this study, the friability percentage for all formulations was under 1%, showing that it is within the allowed limits.

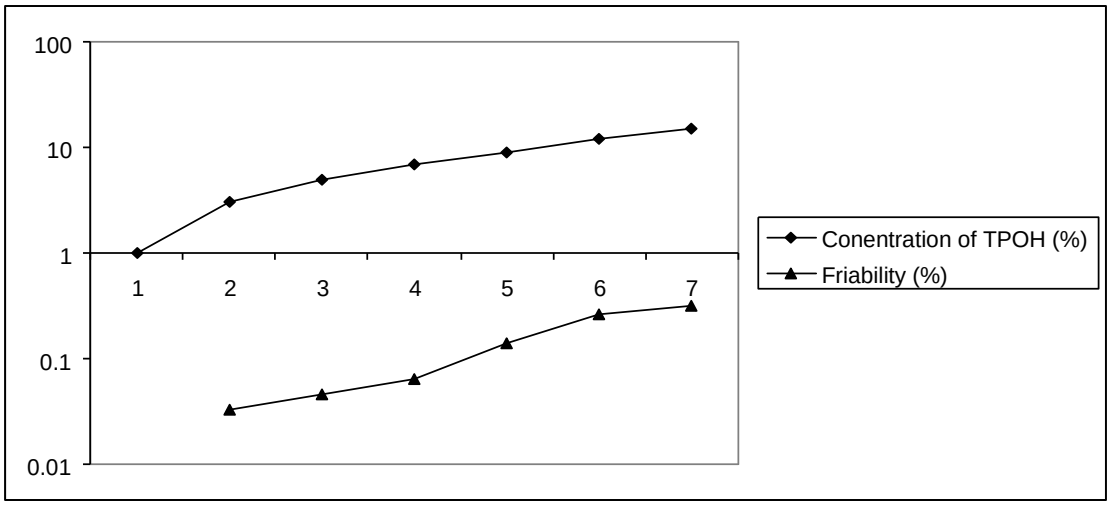


Figure: Effect of TPOH concentration on percentage friability

The formulation with 1% TPOH exhibited a very high wetting time, while the formulation with 15% TPOH showed the lowest wetting time. Comparable results were observed when the wetting test was conducted in 0.1 M HCL and phosphate buffer at pH 7.4. The influence of TPOH concentration on the duration of wetting.

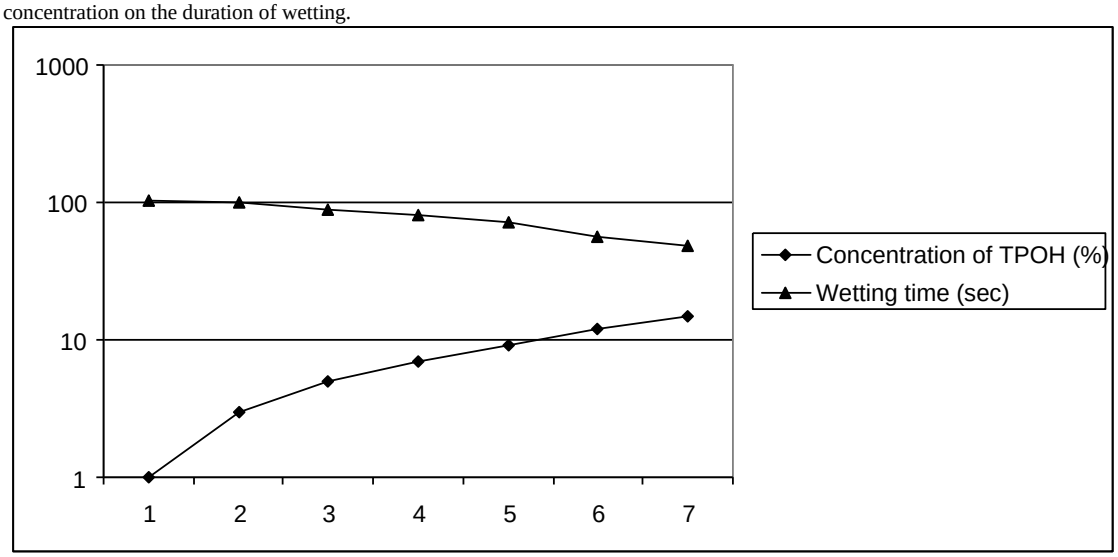


Figure: Effect of TPOH concentration on wetting time

The percentage swelling of the formulations varied from 204.03 ± 5.50 to 303.31 ± 9.15 %. A very important relationship (p=0.0001), characterized by a positive correlation coefficient (R2=0.9881), was observed between the level of TPOH and percentage swelling, suggesting that higher concentrations of TPOH led to an increase in percentage swelling. The highest percentage of swelling was observed in the formulation with 15% of TPOH.

Comparable outcomes were observed when the swelling study was conducted in 0.1 M HCl and phosphate buffer at pH 7.4. The impact of TPOH concentration on swelling (%).

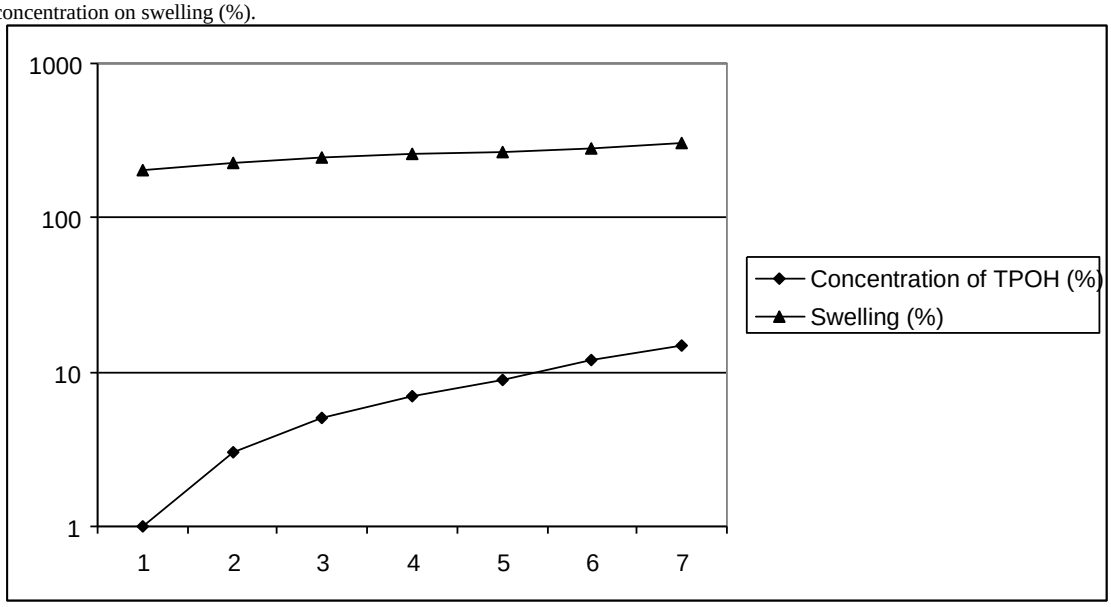


Figure: Effect of TPOH concentration on percentage swelling

CONCLUSION

The results indicate that both treated Plantago ovata husk (TPOH) and pregelatinized suji (Psuji) meet the criteria for disintegrants in fast dissolving tablets. Treated Plantago ovata husk and pregelatinized suji have demonstrated superior disintegrant properties compared to synthetic super disintegrants (like sodium starch glycolate) and those available on the market. Consequently, these formulations can be investigated further in clinical trials and later for commercialization, as they may serve as improved alternatives to current conventional products on the market.

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