"CATALYZING RESPIRATORY: RELIEF INNOVATION IN FAST DISINTEGRATION SALBUTAMOL TABLET FOR ENHANCED THERAPY"

Mohsin Khan Azmat Khan[1], Jay Dnyaneshwar Rathod[2], Sayed Sufiyan Sayed Yaseen[3], Aasim Khan Nazeem Khan[4], Naimoddin Kazi Hakimoddin Kazi[5]

[12345]students

[12345]Ishwar Deshmukh Institute of Pharmacy, Digras, Yavatmal, Maharashtra, India.

Abatract: Salbutamol salphate is used to treat respiratory disorders such as asthma, COPD, and pulmonary hypertension. Salbutamol salphate (SS) is a short-acting beta-2 adrenergic agonist. The first-pass metabolism of the model bronchodilator medication salbutamol salphate (SS) in the liver results in an oral bioavailability of only 50% of the administered dosage. Recent advancements in rapid-dissolving tablets have made dosing easier for juvenile and elderly patients who have difficulty swallowing pills. The goal of this study was to create a quick-dissolving tablet of salbutamol salphate for juvenile respiratory diseases. As dose precision and patient compliance become more significant requirements for long-term therapy, there is a need to design a formulation for this medicine that addresses issues such as difficulty swallowing, annoyance in administration when traveling, and patient acceptance. As a result, the current study was done with the goal of developing a rapid-dissolving tablet of salbutamol salphate that offers a new variety of goods with desirable qualities and intended advantages. Sodium starch glycolate and other superdisintegrants were optimized. Different binders and superdisintegrant concentrations were optimized. Direct compression was used to create the tablets. The tablets' hardness, friability, weight fluctuation, wetting time, disintegration time, and content homogeneity were all examined. The optimized formulation was tested in vitro for dissolving, drug-excipient compatibility, and accelerated stability. It was determined that fast-dissolving tablets of salbutamol salphate were effectively formulated with desirable properties such as quick disintegration, rapid start of action, and improved patient convenience and compliance.

Keywords: Salbutamol salphate, pulmonary hypertension, COPD, Excipient

INTRODUCTION: Despite remarkable advances in medicine delivery, the oral route remains the favored route for remedial agent administration due to its correct cure, low-cost remedy, tone-drug, noninvasive fashion, convenience of administration, and high case compliance(1). Conventional tablets and firm gelatin capsules are the most frequently used lozenge forms. One significant disadvantage of similar cure forms is" dysphagia," or trouble swallowing, which affects over half of the population. As a result, cases don't follow their conventions, resulting in a high rate of resistance and hamstrung treatment. Fast-dissolving medicine delivery styles have lately gained favor and adequacy as innovative drug delivery systems because of their ease of administration and better patient compliance(3). Swallowing traditional capsules may be problematic in some cases, similar to stir-nause, abrupt occurrences of mislike responses or coughing, and a lack of water. Pediatric and senior cases, in particular, have difficulties. Fast-dissolving tablets or orally disintegrating tablets have evolved as an alternate cure type to address similar issues. (4). Recent advances in new medicine delivery systems(NDDS) aim to enhance the safety of a medicine patch while maintaining its remedial efficacity so as to achieve better case compliance. In the" Orange Book," the US Food and Drug Administration Center for Medicine Evaluation and Exploration (CDER) describes an ODT as" a solid lozenge form containing medicinal substances that disintegrates fleetly, generally within a matter of seconds, when placed upon the lingo." ODTs were defined by the European Pharmacopoeia as" uncoated tablets intended to be placed in the mouth where they disperse fleetly before being swallowed" and as tablets that should dissolve within 3 twinkles(6). Fast disintegrating tablets (FDTs) are also known as "quick dissolving," "mouth dissolving," "rapimelt," "presto melts," "orodispersible," "melt in mouth," "quick dissolving," "EFVDAS," or "bouncy medicine immersion system." " Salbutamol is used to treat asthma, bronchospasm, and reversible airway blockage by widening the lugus airway. Salbutamol oral result 2 mg/ 5 ml is applicable for children and

adults who are unfit to use inhalers. Salbutamol salphate presto disintegrating sublingual tablet was made for oral administration using the direct contraction system, which is the most straightforward and cost-effective fashion for producing tablets with good integrity. The time it takes for ODTs to disintegrate is generally one nanosecond, but cases may witness decomposition times ranging from 5 to 30 seconds. It contains numerous of the same excipients as traditional compressed tablets. In this expression, a dissolving agent and a swelling agent are combined with carpeted drug patches to produce a tablet that dissolves in the mouth in less than one nanosecond. In most circumstances, a fast-dissolving medicine delivery system is a tablet that dissolves or disintegrates snappily in the oral cavity when it comes into contact with the slaver, resulting in the release or suspense of the delivered drug. 7) FDT lozenge forms, also known as rapid-fire melt, quick melt, orally disintegrating tablets, and orodispersible systems, are distinguished by their capability to dissolve tablets in the mouth in seconds.

1. MATERIALS AND METHOD:

1) **Salbutamol sulphate:** It's also known as albuterol (MF.C13H21NO3). Salbutamol was discovered in 1966 by a team led by David Jack. Salbutamol is used to treat asthma, bronchospasm, and reversible airway blockage by expanding the lungs' airways. Salbutamol oral solution (2 mg/5 mL) is appropriate for children and adults who are unable to utilize an inhaler to be administered orally.
2) **Sodium starch gyloclate:** It's also known as sodium carboxymethyl starch (MF.C2H3NaO3). It's derived from starch, and with two chemicals, it is utilized as a pharmaceutical-grade dissolving excipient. Sodium starch glycolate quickly absorbs water, causing swelling and the fast breakdown of tablets and granules. It's a disintegrant, a suspending agent, and a gelling agent.
3) **Microcrystalline cellulose:** It's also known as Avicel (MF.C14H26O11). It was discovered in 1955 by Battista and Smith. It is utilized as a disintegrant in tablet manufacture, both in dry compression and wet granulation. It improves medication solubility by hastening tablet breakdown.
4) **Sodium stearyl fumarate:** It's also known as Sodium Octadecyl Fumarate (MF.C22H39NaO4). One of the earliest studies on its functionality was in 1979 by two Swedish researchers, Hölzer and Sjögren, working at Astra Zeneca. Its use as a lubricant and anti-adherent increases powder flowability, minimizes tablet sticking, and promotes tablet
5) **Mannitol:** It's also called D-Mannitol (MF.C6H14O6).Mannitol is one of the low-moldable sugars that promotes rapid breakdown.
6) **Sodium saccharine:** It's also called saccharine or benzosulfimide (MF. C7H5NNaO3S). It was discovered in 1879 by Constantin Fahlberg in the laboratory of Ira Remsen at Johns Hopkins University (Baltimore). It is employed to improve
7) **Talc**: It is also called talcum (Mg3Si4O10(OH)2). It was first discovered on a farm in Madoc, where it is used as a lubricant and diluent, which helps to improve the flow properties of the powder mixture and ensure that the tablets are easily swallowed.

Sr.no.	Name of ingredient	Molecular formula	Uses
1	Salbutamol sulphate	C13H21NO3	To treat asthma, bronchospasm
2	Sodium starch glycolate	C2H3NaO3	As a disintegrant as a suspending agent and as a gelling agent
3	Microcrystalline cellulose	C14H26O11	Improve medication solubility by hastening tablet breakdown
4	Sodium stearyl fumarate	C22H39NaO4	As a lubricant and anti-adherent, promotes tablet dissolving
5	Mannitol	C6H14O6	Promote rapid breakdown
6	Sodium saccharine	C7H5NNaO3S	To improve palatability
7	Talc	Mg3Si4O10(OH)2)	As a lubricant and

2.METHODS:

Excipient Selection and Concentration Optimization:

The disintegration time is the most critical characteristic to optimize in the creation of rapid-dissolving tablets. Fast-dissolving tablets were initially made utilizing several excipients (binders and superdisintegrants) and then analyzed for various factors such as friability, hardness, and disintegration time to determine the ideal combination for fast-dissolving tablet formulation.

The combination with the shortest disintegration time, optimal hardness, and friability was chosen for further research.

Optimization of Superdisintegrant Sodium Starch Glycolate:

For tablets and capsules that require fast disintegration, including the correct superdisintegrant at the proper concentration is essential for good bioavailability. Superdisintegrants shorten disintegration time, which increases the dissolution rate of medication. As a result, the right selection of superdisintegrant and its consistency of performance are essential in the formulation of fast-dissolving dosage forms.

To examine the effect of the kind and concentration of superdisintegrants in Table 1, formulations F1–F6 were created.

The tablets were made using the direct compression process.

In a dry and clean mortar, a weighed amount of salbutamol Salphate was mixed in geometric progression with varied concentrations of superdisintegrants and excipients.

The mixture was then put through sieve number 60 for direct compression. The powder mixture was then compacted.

Optimization of Microcrystalline Cellulose (Avicel PH-102):

As binder, as well as superdisintegrant concentration. The tablets were produced using the direct compression process. Table 2 shows the ingredients of a rapid-dissolving tablet.

In a dry and clean mortar, a weighed quantity of salbutamol Salphate was combined with an optimal concentration of sodium starch glycolate, varied quantities of binders (PVP K-30, MCC), and excipients. The mixture was then run through sieve number 60 for direct compression. The powder blend was then crushed into tablets in a multipunch tablet compression machine utilizing an 8-mm punch.

Salbutamol Sulphate Fast Disintegrating Tablets Final Formulation:

The direct compression technique was used to create fast-disintegrating tablets of salbutamol salphate in mixed form, the formula for which is given in Table. For the stated formulation, the required quantity of each ingredient was taken. In a dry and clean mortar, accurately weighed amounts of salbutamol salphate were cogrinded in geometric progression with optimal concentrations of superdisintegrant and binder with excipients. All of the ingredients were passed through mesh number 60. Consequently, for 5 minutes, talc and sodium stearyl fumarate were added and combined. The excipient mixture was compressed into tablets using an 8-mm punch in a multipunch tablet compression machine.

Sr.no.	Ingredients	F1	F2	F3	F4	F5	F6
1.	Salbutamol sulphate	2	2	2	2	2	2
2.	Sodium starch gyloclate	2(1%)	4(2%)	8(4%)	12(6%)	16(8%)	20(10%)
3.	Microcrystalline cellulose	4	4	4	4	4	4
4.	Sodium stearyl fumarate	3	3	3	3	3	3
5.	Mannitol	181	179	175	171	167	163
6.	Sodium saccharine	5	5	5	5	5	5
7.	Talc	3	3	3	3	3	3

Table 1: Formula for 1 tablet (200 mg) of different concentrations of sodium starch glycolate (data in mg)

content	Salbutamol sulphate(mg)	SSG(mg)	MCC (mg)	Sodium stearyl fumarate	Talc (mg)	Sodium saccharine (mg)	[annitol(mg)
Formulano.							
F1	2	8	-	2	2	5	179
F2	2	8	-	2	2	5	177
F3	2	8	-	2	2	5	175
F4	2	8	-	2	2	5	173
F5	2	8	-	2	2	5	171
F6	2	8	-	2	2	5	169
F7	2	8	-	2	2	5	167
F8	2	8	2	2	2	5	179
F9	2	8	4	2	2	5	177
F10	2	8	6	2	2	5	175
F11	2	8	8	2	2	5	173
F12	2	8	10	2	2	5	171
F13	2	8	12	2	2	5	169
F14	2	8	14	2	2	5	167

Table 2: Formula for 1 tablet (200 mg) for the optimization of microcrystalline cellulose with optimized concentration of sodium starch glycolate.

4. EVALUATION PARAMETER:

a) Weight variation:

The weight variation test was performed by individually weighing 20 tablets using a computerized weighing scale (Ohaus, USA). Calculate the average weight and compare it to the weight of 20 tablets.

b) Thickness:

The thickness of the tablets was measured with a vernier caliper (Indian Caliper Industries, Ambala, India). Three tablets from each batch were utilized, and an average value was determined.

c) Hardness:

Tensile strength (kg/cm2) is the unit of measurement for tablet strength. The tablet crushing load is the force necessary to compress a tablet into halves. A Monsanto Hardness Tester (Perfit) was used to measure it. Three tablets from each formulation batch were randomly selected, and the average reading was recorded.

d) Friability test:

Ten tablets were weighed and placed in a Roche friabilator (Veego, India), which was rotated at 25 revolutions per minute for four minutes. The tablets were removed, cleaned, and reweighed. The friability of the tablets was calculated using the formula shown below.

$$\text{Percentage friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100.$$

e) Test for In Vitro Disintegration:

The tablet's disintegration time was determined in water (37 ±°C) using a Digital Tablet Disintegration Tester (Veego, India). The time it required for the tablet to completely disintegrate with no palpable bulk in the instrument was measured in seconds. For the disintegration time calculations, six tablets from each batch (formulation) were tested.

f) Wetting time:

A Petri dish with 6 mL of distilled water was used. On it was inserted a tablet containing a modest amount of amaranth color. The time it took for the upper surface of the tablet to turn completely red was recorded.

g) Uniformity of Drug Content:

Ten tablets (200 mg) were ground in a mortar and pestle, and the powdered mixture was weighed and mixed in 100 mL of 6.8 pH phosphate buffer solutions. The solution was sonicated, filtered with Whatman filter paper, and diluted with 6.8 pH phosphate buffer before being tested for drug content using a double-beam UV spectrophotometer (UV-1800 Shimadzu) at 276 nm. Each sample was examined three times.

h) Drug-Excipient Compatibility Research:

The purpose of this research was to confirm the drug-excipient interaction. FTIR spectroscopy is extensively used in this research. On an FTIR spectrophotometer (Bruker, USA), the FTIR spectra of pure medicines and compounded FDT-containing medications were recorded. The scanning range was 4000 to 600 cm1, with a resolution of 1 cm1. The scans were examined for the presence of drug primary peaks, drug peak shifting and masking, and the formation of additional peaks due to excipient interaction. This spectral analysis was utilized to determine drug compatibility with the excipients used.

i) Accelerated Stability Studies:

Accelerated stability tests are carried out at 40 ± 2°C (oven) and at ambient humidity, as well as at room temperature (desiccator). The tablets were removed on the 15th and 30th days and tested for hardness, friability, drug content homogeneity, and in vitro disintegration time, which are the most relevant parameters for fast disintegrating tablets.

RESULT:

The current study was undertaken to formulate and evaluate fast-disintegrating tablets of salbutamol salphate using sodium starch glycolate as a superdisintegrant and mannitol as a directly compressible diluent, with sodium saccharin used to improve palatability. Avicel PH 102 was used as a disintegrant and a binder in the formulation. Because this type of microcrystalline cellulose is granular in nature, it has excellent flow qualities. As a sweetening ingredient, sodium saccharin was used to impart a pleasant taste and improve tongue feel.

Sodium stearyl fumarate was used as a lubricant instead of magnesium stearate, not only because of its metallic taste but also because of its water solubility and immediately compressible properties.

CONCLUSION:

A fast-dissolving tablet is a promising strategy for achieving faster medication action and would be preferable to the currently available traditional dose forms. The disintegration time and mechanical strength of the FDT dosage form were well balanced. The study's primary goal was to create a salbutamol salphate fast-dissolving tablet using readily accessible excipients and conventional technologies. According to the findings of the study, a fast-dissolving tablet of salbutamol salphate can be created and commercialized by using readily available pharmaceutical excipients such as superdisintegrants, hydrophilic and swellable excipients, and suitable filler.

REFERENCE:

[1] R. Pahwa, M. Piplani, P. C. Sharma, D. Kaushik, and S. Nanda, ‑Orally disintegrating tablets—friendly to pediatrics and geriatrics,‖ Archives of Applied Science Research, vol. 2, no. 2, pp. 35–48, 2010.

[2] S. Divate, K. Kavitha, and G. N. Sockan, ―Fast disintegrating tablets—an emerging trend,‖ International Journal of Pharma ceutical Sciences Review and Research, vol. 6, no. 2, pp. 18–22, 2011.

[3] R. Panigrahi and S. A. Behera, ―Review on fast dissolving tablets,‖ Webmed Central Quality and Patient,vol. 1, no. 9, pp. 1–17, 2010.

[4] M. Slowson and S. Slowson, ‑What to do when patients cannot swallow their medications,‖ Pharma Times, vol. 51, pp. 90–96, 1985.

[5] S. Corveleyn and J. P. Remon, ―Formulation and produc tion of rapidly disintegrating tablets by lyophilisation using hydrochlorothiazide as a model drug,‖ International Journal of Pharmaceutics, vol. 152, no. 2, pp. 215–225, 1997.

[6] A. K. Nayak and K. Manna, ‑Current developments in orally disintegrating tablet technology,‖ Journal of Pharmaceutical Education and Research, vol. 2, no. 1, pp. 21–34, 2011.

[7] S. A. Sreenivas, P. M. Dandagi, A. P. Gadad et al., ‑Orodis persible tablet: new-fanged drug delivery system—a review,‖ Indian Journal of Pharmaceutical Education and Research, vol. 39, no. 4, pp. 177–181, 2005.

[8] D. Bhowmik, B. Chiranjib, K. Pankaj, and M. R. Chandira, ‑Fast dissolving tablet: an overview,‖ Journal of Chemical and Pharmaceutical Research, vol. 1, no. 1, pp. 163–177, 2009.

[9] B. G. Prajapati and N. Ratnakar, ―A review on recent patents on fast dissolving drug delivery system,‖ International Journal of PharmTech Research, vol. 1, no. 3, pp. 790–798, 2009.

[10] M. Swamivelmanickam, R. Manavalan, and K. Valliappan, ‑Mouth dissolving tablets: an overview,‖ International Journal of Pharmaceutical Sciences and Research, vol. 1, no. 12, pp. 43–55, 2010.

[11] K. D. Tripathi, Essential of Medical Pharmacology, pp. 216–217, Jaypee Brothers Medical, New Delhi, India, 6th edition, 2008.

[12] S. B. Jadhav, D. R. Kaudewar, G. S. Kaminwar, A. B. Jadhav, R. V. Kshirsagar, and D. M. Sakarkar, ‑Formulation and evaluation of dispersible tablets of diltiazem hydrochloride,‖ International Journal of PharmTech Research, vol. 3, no. 3, pp. 1314–1321, 2011.

[13] V. Metker, A. Kumar, N. Pathak, K. Padhee, and S. Sahoo, ‐For mulation and evaluation of orodispersible tablets of lornoxi cam,‖ International Journal of Drug Development and Research, vol. 3, no. 1, pp. 281–285, 2011.

[14] A. Arya, S. Sharma, J. Kumar, A. Chandra, and P. Jaiswal, ‐Formulation and evaluation of mouth dissolving tablets of ranitidine HCL,‖ International Journal of Pharm Tech Research, vol. 2, no. 2, pp. 1574– 1577, 2010.

[15] R. B. Parmar, A. H. Baria, H. M. Tank, and S. D. Faldu, ―Formulation and evaluation of domperidone fast dissolving tablets,‖ International Journal of PharmTech Research, vol. 1, no. 3, pp. 483–487, 2009.

[16] B. Senthilnathan and A. Rupenagunta, ―Formulation devel opment and evaluation of venlafaxine hydrochloride orodis persible tablets,‖ International Journal of Pharmaceutical Sci ences and Research, vol. 2, no. 4, pp. 913–921, 2011.

[17] P. B. Anjankumar, M. Nazmuddin, U. Kulkarni, and R. C. Hariprasanna, ―Formulation and evaluation of lornoxicam fast dissolving tablet,‖ International Research Journal of Pharmacy, vol. 2, no. 4, pp. 130–133, 2011.