Formulation And Evaluation of Fast Disintegrating Tablet of Valacyclovir Hydrochloride Using Synthetic superdisintegrants.

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ABSTRACT

Valacyclovir is an antiviral drug used to treat herpes simplex virus as well as varicella zoster virus. It is a BCS class III medication. To accomplish quick dose form dissolution and disintegration, the valacyclovir rapid dissolving tablet was developed. To accomplish this, super disintegrants were utilised to speed up the dissolving process and lengthen the disintegration period, such as croscarmellose sodium, sodium starch glycolate, and crospovidone. The fast-disintegrating tablets were formulated by direct compression method and all the precompression and post compression parameters were evaluated. After incorporating super disintegrants like croscarmellose sodium, crospovidone and sodium starch glycolate.

orally disintegrating tablet formulation of valacyclovir was prepared using direct compression technique. Nine formulations were formulated out of which, tablet containing croscarmellose sodium gave superior in vitro dispersion time and drug release. It is concluded that super disintegrants could be used to prepare fast disintegrating valacyclovir tablets via direct compression.

Keywords: Valacyclovir, fast-disintegrating tablets, crospovidone

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INTRODUCTION

The innovative method of medication delivery via the oral route is oral disintegration tablets. The most often used dosage form is the tablet since it is compact, convenient to self-administer, and inexpensive to produce. The majority of patients, especially the elderly and young children, struggle to swallow pills and capsules, making it impossible for them to take their medications as prescribed. Such a condition affects about 50% of the population, leading to a high prevalence of noncompliance and infectious treatment. Fast dissolving tablets and orally dissolving tablets have become alternate dose forms to address these issues. (1)

The solid unit dose form known as an oral disintegrating tablet dissolves or disintegrates quickly in the mouth without chewing or drinking. It offers excellent stability, precise dosage, simple manufacture, compact packaging, and patient-friendly handling. (2)

A solid dosage form containing a medication or active component that, when put on the tongue, quickly dissolves, often in a couple of seconds. Oral dissolving tablets have been found to be the most effective treatment for people with mental conditions etc. These goods may also be referred to as Rapid Melts, Oro- dispersible, porous tablets, or swiftly dissolving tablets.. (3)

VIRUS

Virus is a microscopic (infectious) creatures, which grows inside living cells. All living organisms either plants or animals or any microscopic organisms like bacteria, are vulnerable to viral infections. The most prevalent type of living thing on Earth is a virus, which may be found in almost every environment. The study of viruses is known as virology, which is a subfield of microbiology.

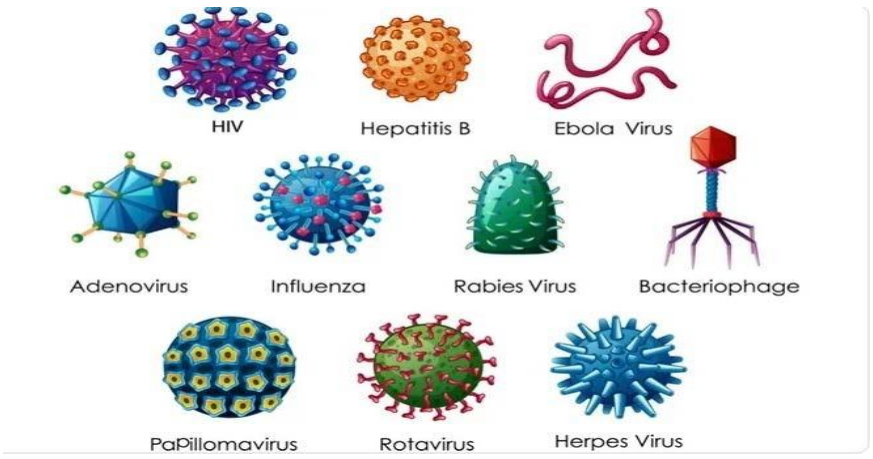


Fig 1. Different types of viruses

ANTIVIRAL DRUGS

Viral infections are treated with drugs from the antiviral drug class. While the majority of antivirals focus on specific viruses, a broad-spectrum antiviral is effective against a range of viruses. In contrast to most antibiotics, antiviral drugs inhibit the growth of the pathogen they are designed to treat.

\Since the bulk of antivirals are believed to be largely harmless for the host, infections can

be treated with them. Viricides, in contrast, do not work as pharmaceuticals but rather deactivate or kill viral particles inside or outside the body. Some plants, such as eucalyptus and Australian tea trees, naturally produce viricides. (4)

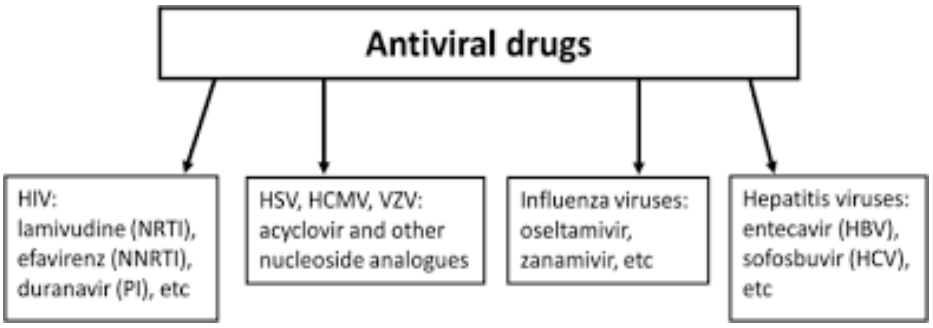
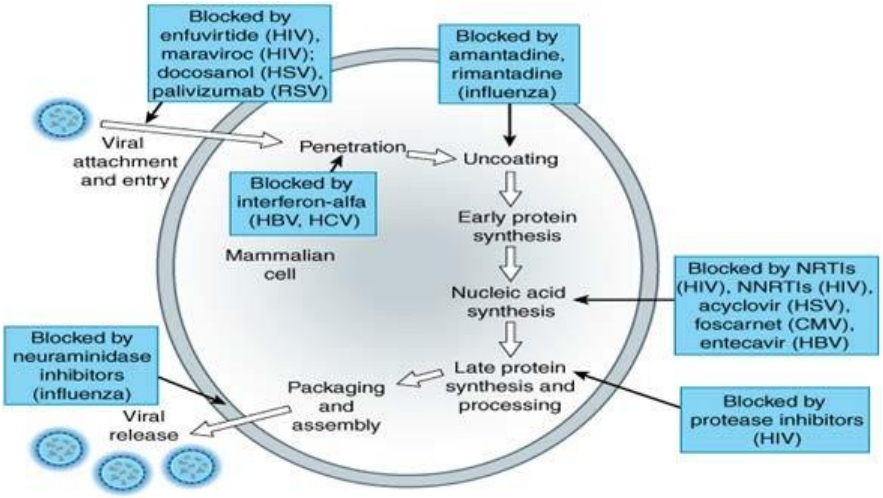


Fig 2 Antiviral drugs

Mechanism of action:



MATERIALS

Valacyclovir hydrochloride, microcrystalline cellulose, talcum, fumed silicon dioxide etc.

Method

Direct compression method of tablet formulation.

The entire list of ingredients were weighed accurately after being passed through sieve no. 60 and dried for one hour at 50^{o}C.

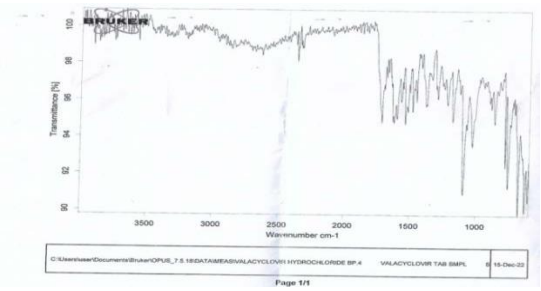
Ingredients(mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Valacyclovir	500	500	500	500	500	500	500	500	500
Croscarmellose sodium	20	40	80	-	-	-	-	-	-
Sodium starch glycollate	-	-	-	20	40	80	-	-	-
Crospovidone	-	-	-	-	-	-	20	40	80
Microcrystalline cellulose	266	246	206	266	246	206	266	246	206

Talcum	5	5	5	5	5	5	5	5	5
Colloidal silicon dioxide	5	5	5	5	5	5	5	5	5
Aspartame	2	2	2	2	2	2	2	2	2
Flavor	2	2	2	2	2	2	2	2	2

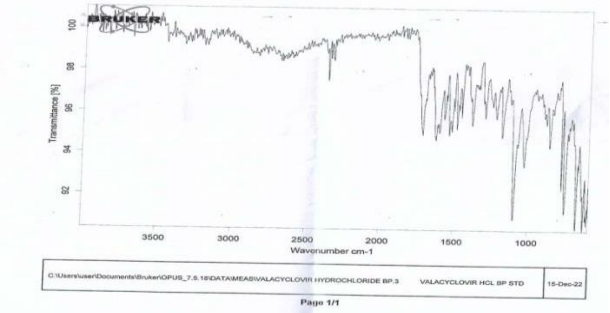
RESULTS AND DISCUSSION

1.1 PREFORMULATION STUDIES

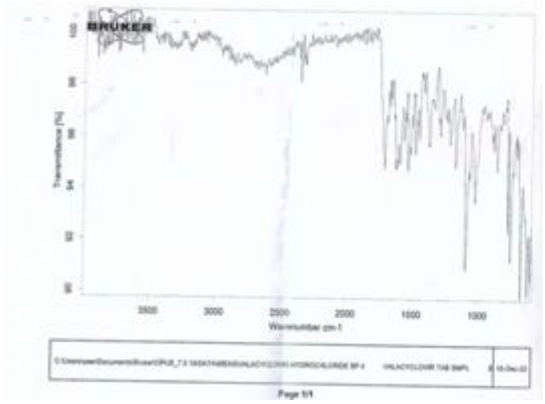
5.1.1 Compatibility studies The FTIR Graphs



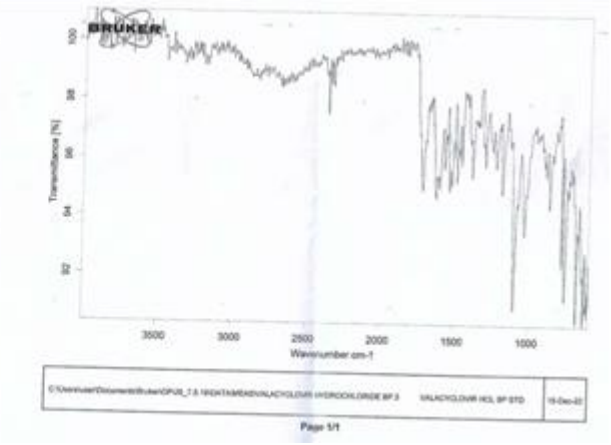
Graph-1 FTIR of valacyclovir tablet



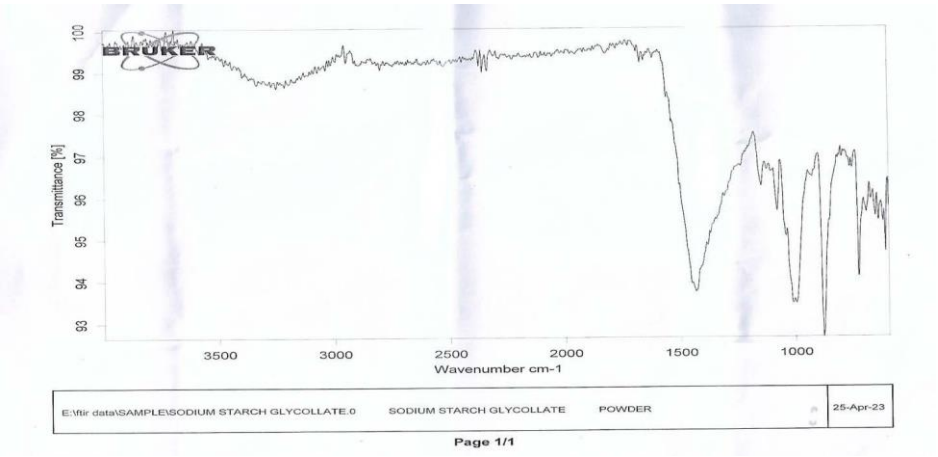
Graph-2 FTIR of valacyclovir drug



Graph 3 FTIR of crospovidone



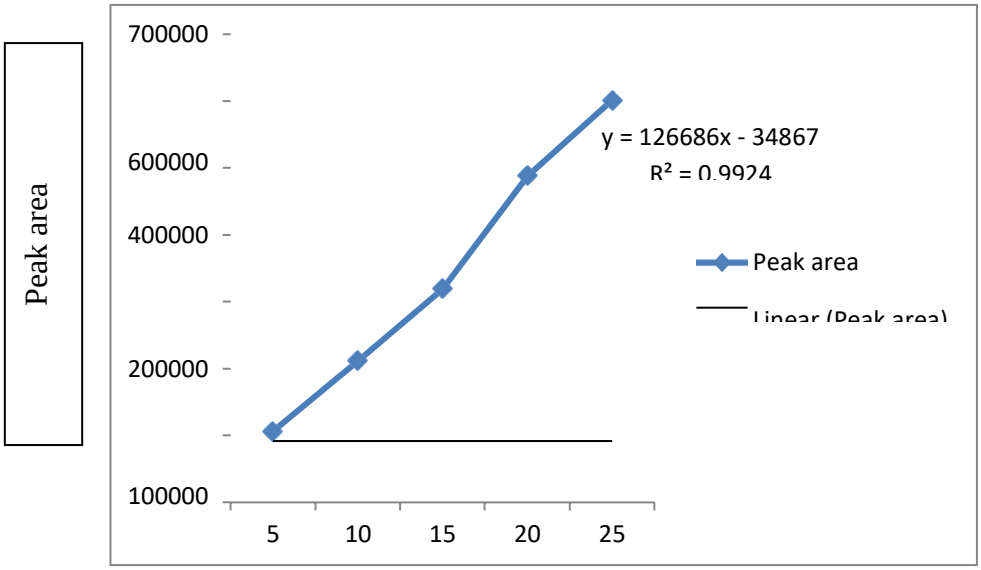
Graph 4 FTIR Of CCS



Graph 5 FTIR of SSG

Standard calibration curve of valacyclovir

To prepare the series of concentrations (5,10,15,20,25g/ml), weigh 60 mg of the valacyclovir standard and dissolve in mobile phase to make up the 50 mililitre. The volume should then be adjusted using the same solvent. The peak is noted at 254 nm

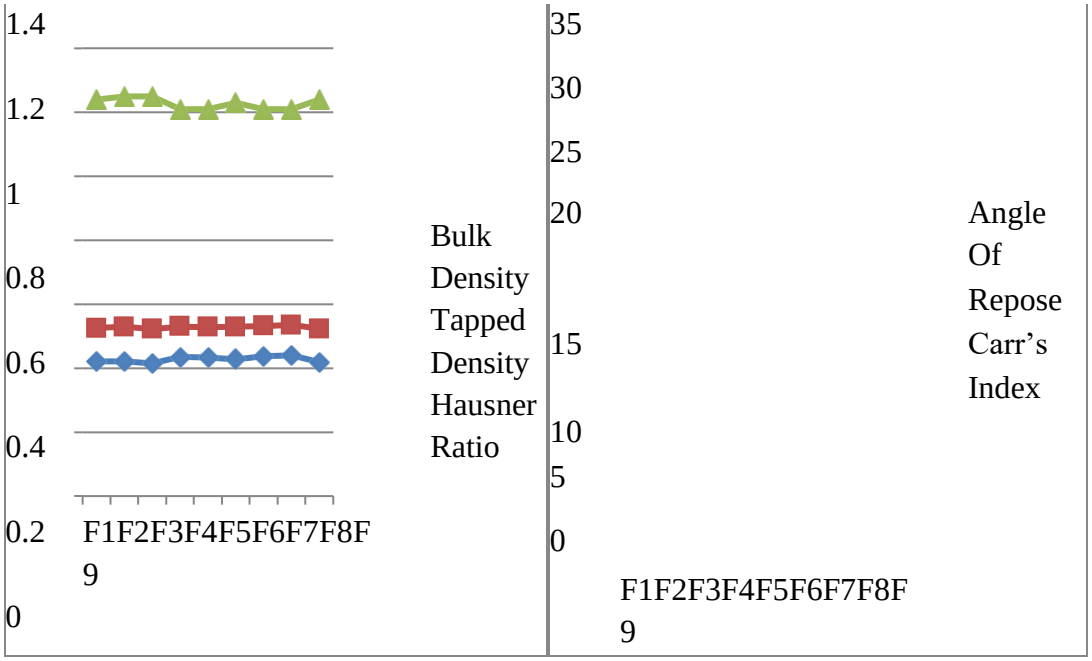


Preformulation studies

Table 1 – Preformulation results

Formulation	Bulk Density ±SD	Tapped Density ±SD	Angle Of Repose ±SD	Carr'sIndex ±SD	HausnerRatio ±SD
F1	0.421±0.02	0.525±0.04	28.26±2.12	19.81±0.34	1.24±0.03
F2	0.422±0.03	0.529±0.05	29.42±2.15	20.22±1.24	1.25±0.05
F3	0.415±0.04	0.522±0.01	32.44±2.16	20.49±1.65	1.25±0.07
F4	0.435±0.01	0.530±0.02	30.47±2.12	17.92±1.22	1.21±0.01
F5	0.433±0.03	0.528±0.03	32.35±2.14	17.99±0.57	1.21±0.01
F6	0.428±0.02	0.529±0.03	31.05±2.13	19.09±0.66	1.23±0.04
F7	0.437±0.05	0.532±0.04	29.67±2.16	17.85±1.45	1.21±0.03
F8	0.440±0.03	0.535±0.02	29.88±2.12	17.75±1.19	1.21±0.03
F9	0.419±0.02	0.523±0.02	30.45±2.17	19.88±0.65	1.24±0.05

Based on the above parameters, the composites exhibited favorable flow characteristics, while the excipients had no noticeable impact.

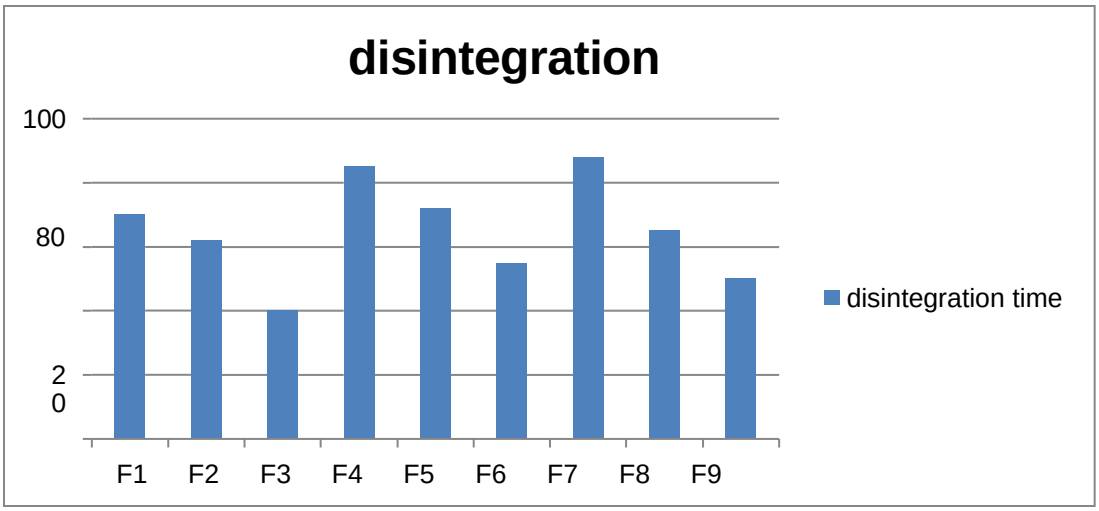


Graph 7 Preformulation Parametrs

Post Formulation Studies

Table 2 – Post formulation results

Formulation	Thickness (MM)	Hardness (Kg/Cm^2)	Friability (%)	Disintegration time (sec)
F1	4.8±0.02	3.2	0.33	70±2
F2	4.9±0.05	4.1	0.32	62±4
F3	5.0±0.01	3.6	0.42	40±1
F4	5.0±0.06	3.5	0.45	85±3
F5	4.9±0.02	3.2	0.22	72±5
F6	5.0±0.01	3.9	0.39	55±2
F7	5.0±0.02	3.4	0.51	88±1
F8	4.9±0.06	4.2	0.36	65±2
F9	5.1±0.03	3.1	0.47	50±1



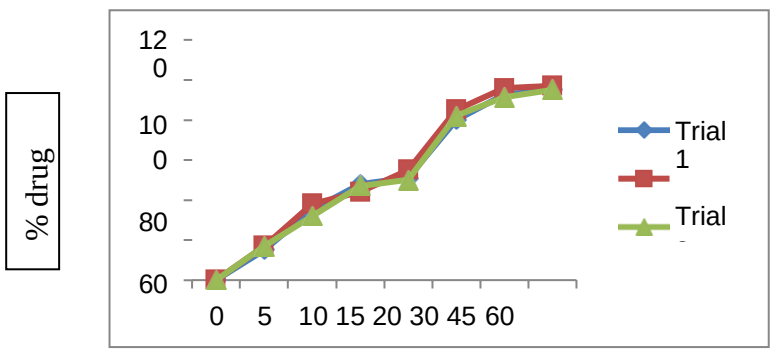
Graph 8 Disintegration Time

According to the previously stated post compression parameters, all formulations are determined to be within the limit

Dissolution Test

Table -3 - drug release of formulation (F1) of valacyclovir

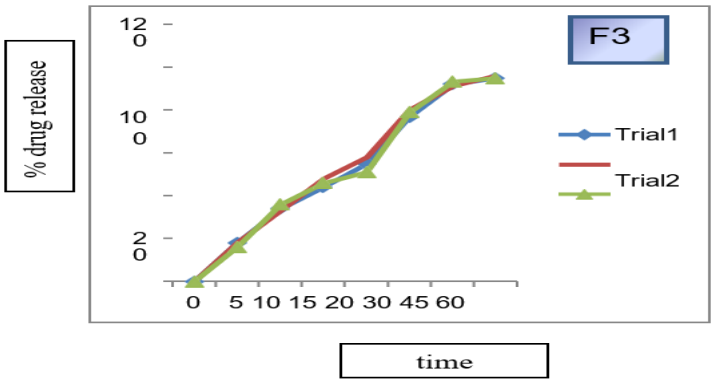
TIME (Min)	Trial1 (% drug release)	Trial2 (% drug release)	Trial3 (% drug release)	Mean of trial	±Std.Dev.
0	0.0	0.0	0.0	0.0	0.0
5	15	17	17	16.33	1.15
10	35	36	32	34.33	2.08
15	48	44	47	46.33	2.08
20	51	55	50	52.00	2.64
30	80	85	82	82.33	2.51
45	92.6	95.8	91.2	93.20	2.35
60	95	97	95	95.66	1.15



Graph 9 % drug release of F1

Table 5 – release of drug of F3 formulation

TIME (Min)	Trial1 (% drug release)	Trial2 (% drug release)	Trial3 (% drug release)	Mean of trial	±Std.Dev.
0	0.0	0.0	0.0	0.0	0.0
5	18	18	16	17.33	1.15
10	34	33	36	34.33	1.52
15	44	48	46	46.00	2.00
20	55	58	51	54.66	3.51
30	77	80	79	78.66	1.52
45	92.1	91.1	93.4	92.20	1.15
60	95	96	95	95.33	0.57

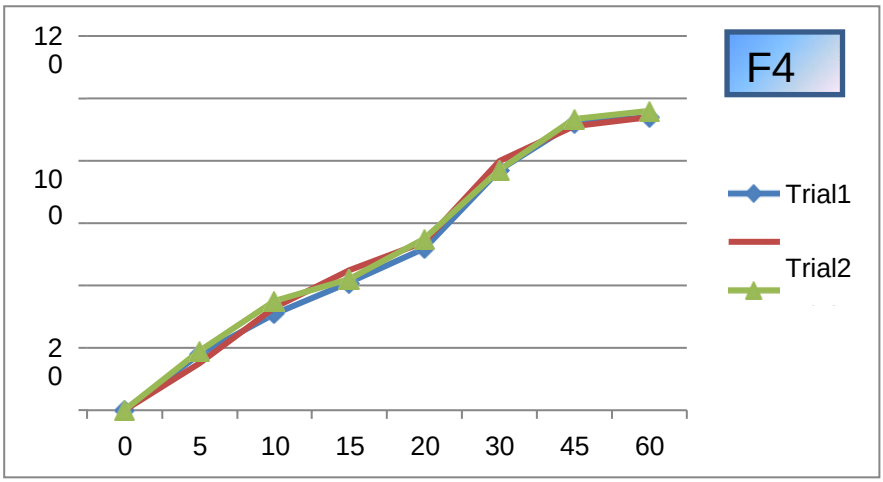


Graph 13 - % drug release of F3

Table 6 - Release of Drug of (F4) valacyclovir

TIME (Min)	Trial1 (% drug release)	Trial2 (% drug release)	Trial3 (% drug release)	Mean of trial	±Std.Dev.
0	0.0	0.0	0.0	0.0	0.0
5	18	15	19	17.33	2.08
10	31	33	35	33.00	2.00

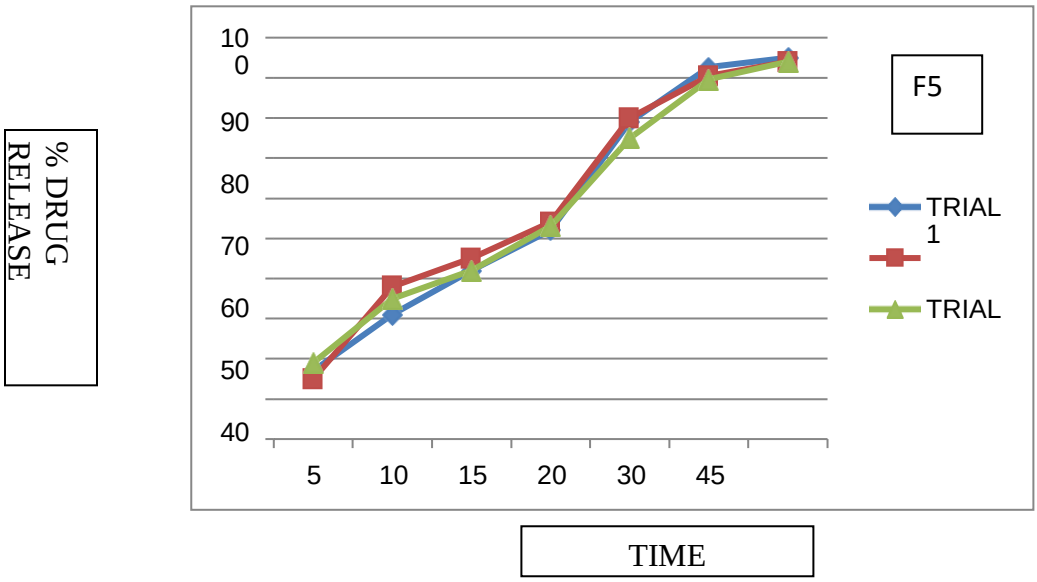
15	41	45	42	42.67	2.08
20	52	54	55	53.67	1.52
30	77	80	77	78.00	1.73
45	92.1	91.1	93.4	92.20	1.15
60	94	94	96	94.66	1.15



Graph15

Table 7 – Release of Drug of formulation F5

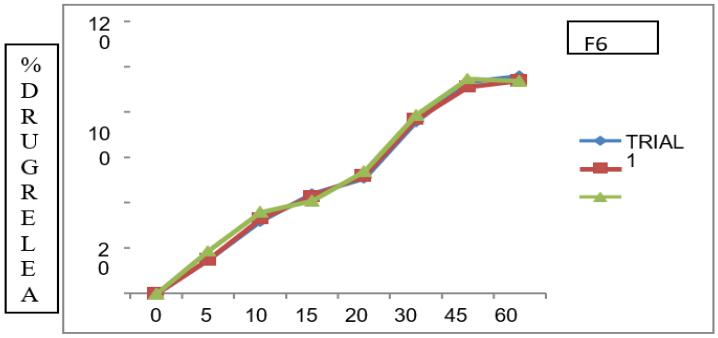
TIME (Min)	Trial1 (% drug release)	Trial2 (% drug release)	Trial3 (% drug release)	Mean of trial	±Std.Dev.
0	0.0	0.0	0.0	0.0	0.0
5	17	15	19	17	2
10	31	38	35	34.6	3.5
15	42	45	42	43	1.7
20	52	54	53	53	1
30	79	80	75	78	2.6
45	92.6	90.4	89.6	90.8	1.5
60	95	94	94	94.3	0.5



Graph17 % drug release of F5

Table 8 – Release of Drug of formulation F6

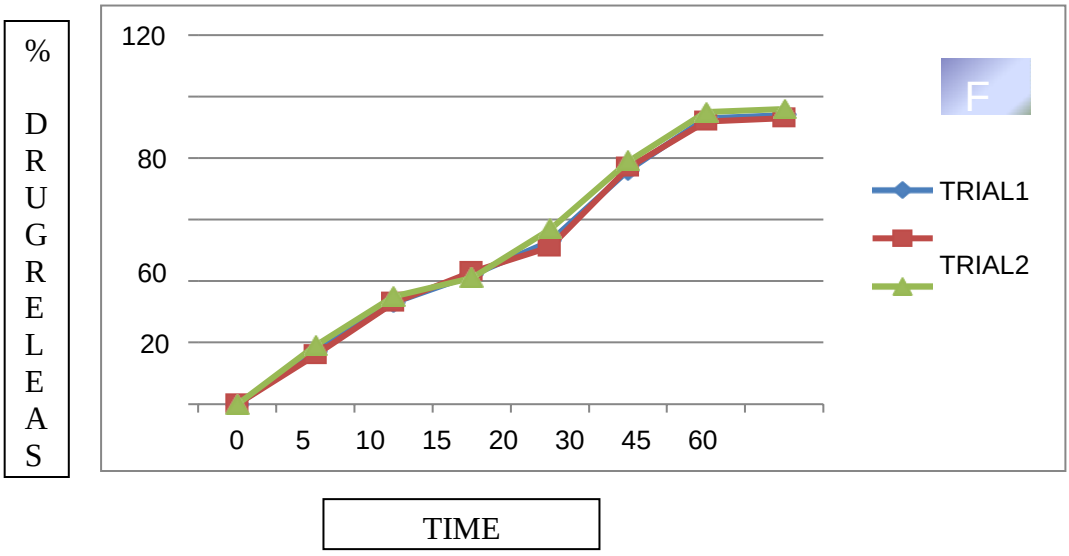
TIME (Min)	Trial1 (% drug release)	Trial2 (% drug release)	Trial3 (% drug release)	Mean of trial	±Std.Dev.
0	0.0	0.0	0.0	0.0	0.0
5	15	15	19	16.33	2.30
10	32	33	36	33.66	2.08
15	44	43	41	42.66	1.52
20	51	52	54	52.33	1.52
30	76	77	79	77.33	1.52
45	93.3	91.2	95	93.16	1.90
60	96	94	94	94.66	1.15



Graph 19 - % drug release of F6

Table 9 - Release of Drug of F7

TIME(Min)	Trial1 (% drug release)	Trial2 (% drug release)	Trial3 (% drug release)	Mean of trials	±Std. Dev.
0	0.0	0.0	0.0	0.0	0.0
5	17	16	19	17.3	1.5
10	33	33	35	33.6	1.1
15	42	43	41	42.0	1.0
20	53	51	57	53.6	3.0
30	76	77	79	77.3	1.5
45	92.9	91.9	94.9	93.2	1.5
60	94	93	96	94.3	1.5



Graph 21 - % drug release of F7

Table 10 – release of drug of formulation F8

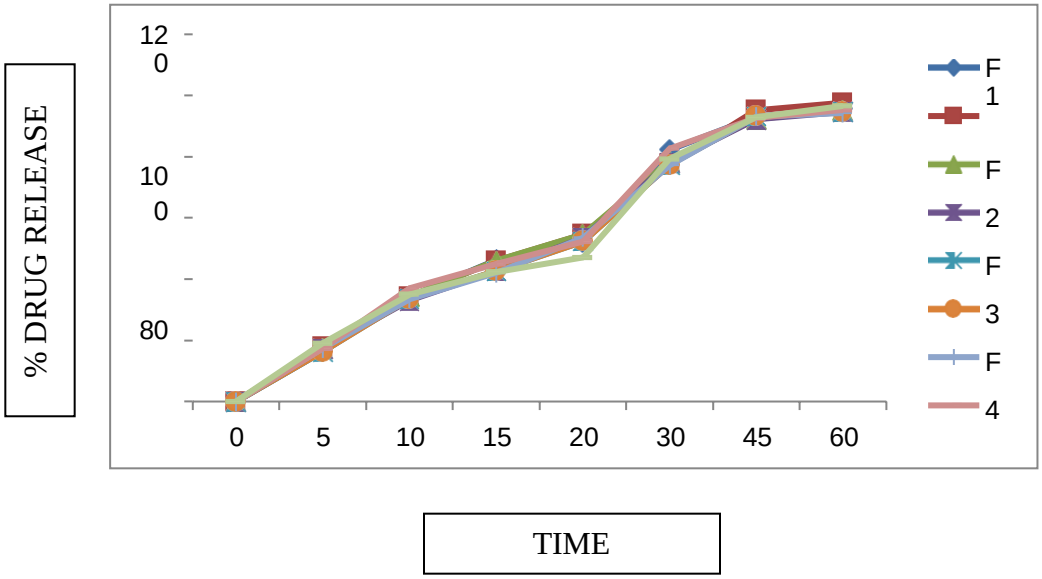
TIME(Min)	Trial1 (% drug release)	Trial2 (% drug release)	Trial3 (% drug release)	Mean of trials	±Std. Dev.
0	0.0	0.0	0.0	0.0	0.0
10	16	18	18	17.3	1.1

10	35	40	36	37.0	2.6
15	45	44	46	45.0	1.0
20	53	55	50	52.3	5.8
30	79	85	84	82.7	3.2
45	90.4	92.8	94.6	92.6	2.1
60	94	95	97	95.3	1.5

Table 12 - COMPARATIVE STUDY OF % DRUG RELEASE OFVALACYCLOVIR FAST

DISINTEGRATINGTABLETS:

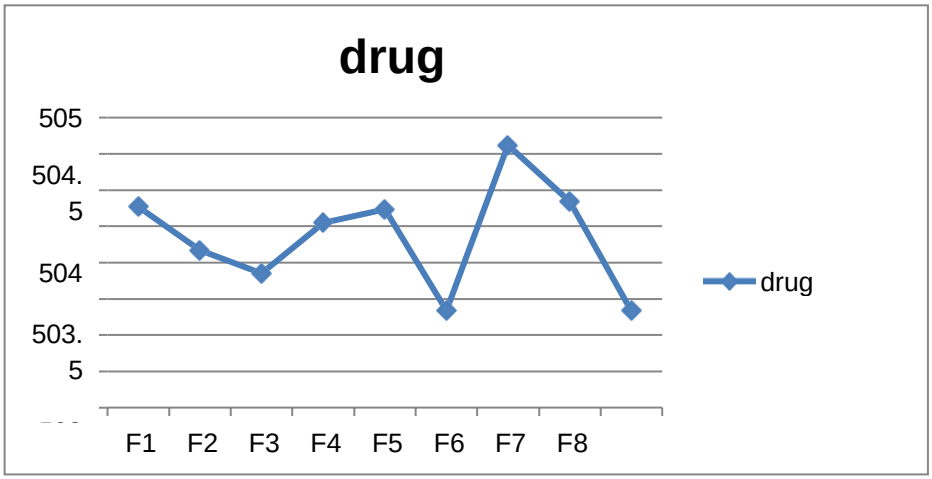
TIME	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
5	16.33	18.00	17.33	17.33	16.33	16.33	17.3	17.3	19.0
10	34.33	34.33	34.33	33.00	33.66	33.66	33.6	37.0	35.0
15	46.33	46.00	46.00	42.67	42.66	42.66	42.0	45.0	42.3
20	52.00	54.66	54.66	53.67	52.33	52.33	53.6	52.3	47.0
30	82.33	77.66	78.66	78.00	77.33	77.33	77.3	82.7	79.3
45	93.20	95.23	92.20	92.20	93.16	93.16	93.2	92.6	92.8
60	95.66	97.66	95.33	94.66	94.66	94.66	94.3	95.3	96.6



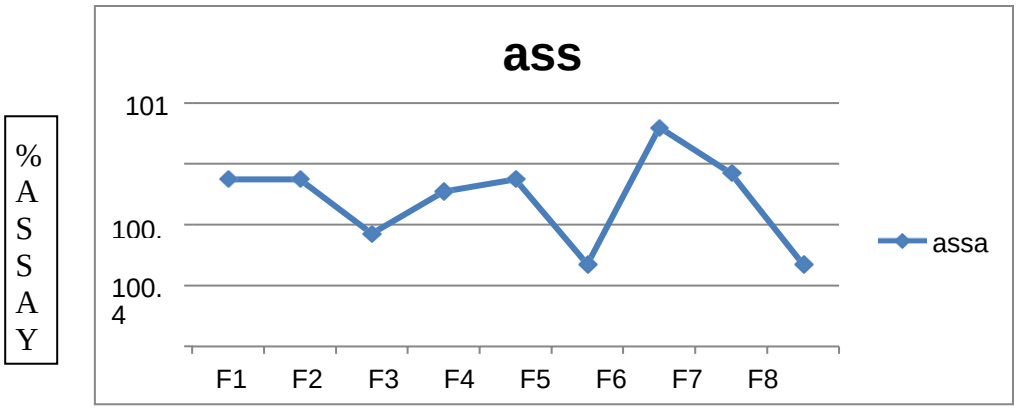
Graph 27 comparitive in vitro drug releases of all formulations

Table 13 – Assay of formulations of valacyclovir fast disintegrating tablets

S.No	Standard	Test 1	Test 2	ASSAY(%)	DRUG CONTENT (mg)
1.	7478867	7475226	7461756	100.75	503.77
2.	7478867	7471039	7468620	`100.63	503.17
3.	7478867	7478139	7475993	100.57	502.85
4.	7478867	7476232	7476037	100.71	503.55
5.	7478867	7471010	7481189	100.75	503.73
6.	7478867	7470892	7475262	100.47	502.34
7.	7478867	74738182	7469423	100.92	504.62
8.	7478867	7477350	7469593	100.77	503.84
9.	7478867	7447082	7473406	100.47	502.33
Mean	7478867	14945016.89	7472364	100.6763	503.3556
S.D	0	22422438.89	5666.795	0.158829	0.754687
% RSD	0	150.0328776	0.075837	0.157763	0.149931



Graph 38 - drug content



Graph 39 - % assay

DISCUSSION

Valacyclovir is accessible as uncoated and floating tablets, but because it is used to treat herpes, it is also required to develop a fast-acting drug that the patient may swallow easily and that starts working immediately away. It must dissolve fast in order to be effective in treating HSV since it is a prodrug and takes time to change into acyclovir.An effective anti-herpes medication called valacyclovir aids in the treatment of herpes infections. To solve these issues, an oral disintegrating dosage form must be created, ideally one that dissolves quickly in saliva and may be taken anytime, anyplace, without water.

Valacyclovir oral disintegrating tablets made by direct compression technique employing various quantities of SSG, crospovidone, and CCS. The preparation and evaluation of 9 formulations (F1 to F9) for the post-compression investigation.

The medication release rate increased when super disintegrants were utilised at varied concentrations, according to the results of all formulations. There was no discernible difference in the drug content, weight fluctuation, friability, or hardness. For F1-F9 formulations, the disintegration period was discovered to 40 - 80 sec & the drug released from F1- F9 vary from 89.5% - 96.9%.

The formulation F3 with croscarmellose sodium as a superdisintegrant had the shortest disintegration time of 40 seconds while the formulation F2 demonstrated the highest drug release within 45 minutes (96.9%). The findings indicate that the disintegration time was prolonged in the way described below.Croscarmellose sodium >Sodium starch glycolate >crospovidone Above study shows that F3 formulation shows the best drug content of 100.57%.

CONCLUSION

Different superdisintegrants were used in various ratios to generate the oral disintegrating Valacyclovir tablets. Using Valacyclovir and the superdisintegrant croscarmellose, the F3 formulation exhibits the highest drug content, the shortest disintegration time and the greatest invitro percentage medication release, according to the study's results.The goal of the investigation is to develop and assess a fast disintegrating tablet containing the antiviral (antiherpes) medication valacyclovir. The purpose of the current study is to manufacture a dispersible tablet of the antiviral drug valacyclovir hydrochloride that dissolves quickly in the mouth and shortens the time it takes for its effects to take effect. MCC was chosen as the super disintegrant, along with sodium starch glycolate, crosspovidone, and croscarmellose sodium. A sweetening substance called aspartame, a lubricant called talcum, and a glident called aerosil.

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