Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(6), 3485-3492| ISSN:2251-6727

Comparative Dissolution Profile Study Of Aciclovir In Solid Dosage Formulations

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(Received: 07 October 2023 Revised: 12 November Accepted: 06 December)

KEYWORDS:-
Aciclovir tablet, Dissolution, Difference factor, Similarity factor, high solubility, low permeability.

ABSTRACT:
This study compares the in vitro efficacy of two distinct brands of acyclovir tablets with the same strength—ACYPROVE-200 (Aciclovir Tablet IP) and ZOVIRAX TABLETS (Aciclovir Tablet IP200MG).Friability, hardness, thickness, solubility, and weight fluctuation tests are only a few of the many comparisons. The most crucial test that enables us to ascertain the precise concentration of the active ingredient (acyclovir) in every capsule and the quantity of medication discharged from these formulations is the dissolution test.Because of its great solubility and limited permeability, the medication aciclovir is categorized as Class III in the BCS classification.Dissolution tests were conducted in acid medium, pH 4.5 buffer medium, and pH 6.8 buffer medium in this study. The dissolution rate is determined by measuring the amount of medication released at intervals of 10, 15, and 30 minutes. The results also show the similarity and difference between the two products.The study concludes that there is a range of 0–15 and 50–100 for the Difference factor (f1) and Similarity factor (f2) between "ACYPROVE-200 (Aciclovir Tablet IP) and ZOVIRAX TABLETS (Aciclovir Tablet IP200MG)."

INTRODUCTION :

Drug development has acknowledged the importance of in vitro dissolution. It can serve as a stand-in for the evaluation of bioequivalency in specific situations. Drug dissolution from immediate and modified release dose forms is described by a number of theories and kinetics models. The quantity of drug dissolved from the pharmaceutical dosing system is represented by the function ft, which is a function of t (time), in a number of models that depict drug dissolution profiles. Using a general equation that quantitatively translates the dissolution curve in function of some parameters linked to the pharmaceutical dosage forms facilitates the quantitative interpretation of the values acquired in the dissolution assay. In certain situations, such as zero order kinetics, that equation can be inferred from a theoretical study of the process. The majority of the time, there is no theoretical foundation for tablets, capsules, coated forms, or prolonged release forms; instead, more suitable empirical formulae are often employed. One medication that is used to treat herpes simplex virus infections is acyclovir (HSV). HSV encephalitis and genital herpes can be treated with it, according to FDA approval. Mucocutaneous herpes zoster (shingles), varicella zoster (chickenpox), and herpes zoster (shingles) are not FDA-approved indications.[/2][/3] The first-line treatment for HSV encephalitis is acyclovir. At this time, there are no further drugs that are recommended to treat this illness.*[4] A systematic evaluation on the effectiveness of this disease/treatment combination has not been conducted, despite the fact that acyclovir has been used for a long time to treat HSV encephalitis. The mortality rate is the main consequence of the current systematic reviews that investigate its safety and efficacy. The quality of life is a secondary outcome measure.In

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pediatric patients, oral acyclovir and topical steroids have been demonstrated to be effective treatments for HSV keratitis.(6).Treatment for the herpes simplex virus-induced stromal keratitis with ulceration can be clinically challenging. Two patients' responses to intravenous acyclovir treatment were studied by Pisitpayat P. et al. for effectiveness.[7]
By using polymerase chain reaction (PCR) analysis on corneal scraping samples, the diagnosis was verified. Herpes simplex virus type 1 affected one patient, whereas type 2 affected the other.

Oral acyclovir was the initial treatment for the patient's herpes simplex virus-1 corneal infection. The patient was moved to intravenous acyclovir, though, as the ocular infection became more serious. The infection on the cornea got better over time. Intravenous acyclovir treatment was administered for the patient's herpes simplex virus-2 corneal infection. The infection on the cornea cleared up. A 100% autologous serum treatment was necessary for the patient's epithelial lesion until it healed, though. To avoid reinfection of the cornea, both patients were treated prophylactically with oral acyclovir. Acyclovir is sometimes used to treat eczema herpeticum in patients infected with the HIV virus. Additionally, infections of the mouth, nose, eyes, and skin are prevented with its use. In the absence of treatment, eczema herpeticum is uncommon but progresses quickly. Admitted patients should receive intravenous acyclovir treatment if they have systemic symptoms, decreased oral intake, or complete involvement.(8) Moreover, oral hairy leukoplakia is treated with acyclovir.In [9]10].Treating myelopathy caused by varicella-zoster infection has shown promise when using acyclovir. A notable resolution of symptoms was observed in the majority of patients within two months in a small case series involving individuals diagnosed between 1994 and 2014 with varicella-zoster virus (VZV) and myelopathy verified by MRI.In [11]Both visceral disseminated VZV infection (the hallmark signs of which include abdomen and lack of skin) and brachial plexus neuritis owing to VZV infection[12]. Acyclovir prophylactic medication may be beneficial in treating reactivation of varicella-zoster and herpes simplex virus in recipients of hematopoietic stem cell transplantation. Organ recipients who test positive for HSV-1 and HSV-2 should also think about taking acyclovir prophylactically.13] As a result of this action, diseases caused by these viruses have diminished. On the other hand, a breakthrough infection might happen. Not unexpectedly, individuals who have stopped taking acyclovir treatment frequently get HSV and VZV infections.Reference [14]Juvenile-onset recurrent respiratory papillomatosis is another example of acyclovir use as a preventive measure. Oral acyclovir was used as a postoperative adjuvant in a prospective observational research with twenty-one patients. It has been demonstrated to reduce papilloma recurrence, which in turn reduces the need for additional surgeries and the hazards involved with such procedures.[15]Cerebelllitis is one of the several side effects of VZV infections. It's also been demonstrated that treating the underlying infection reduces the risk of complications. One case report from 2019 details a patient who had truncal ataxia. The patient no longer had cerebellitis or neurologic impairment following intravenous acyclovir treatment. [16]

Mechanism of Action:
An antiviral drug called acyclovir combines with viral DNA to stop additional synthesis. After being converted to acyclovir triphosphate by viral and cellular enzymes, it inhibits the synthesis of new DNA and the replication of existing viruses. Synthetic purine nucleoside analog acyclovir has been shown to exhibit inhibitory effect against varicella-zoster virus and herpes simplex virus types 1 (HSV-1), 2 (HSV-2), both in vitro and in vivo.[17]With the exception of corneal infections, acyclovir-resistant herpes simplex viruses (HSV) are rare (<1%) in immunocompetent people. Immunocompromised patients, such as those undergoing hematopoietic stem cell transplantation, are more likely to harbor acyclovir-resistant HSV.[18]

AIM AND OBJECTIVE:
As per the BCS classification the Aciclovir drug is classified under ClassIII since the drug is high solubility,low permeability.

OBJECTIVE OF THE WORK:
1.To check whether the excipients used in the formulation of the Aciclovir tablets affect,the BCS classification(solubility)of the drug or not
2.Dissolution test in Acid medium, pH4.5 buffer medium and pH buffer 6.8 mediumare tested for two markets available oral solid dosage form of the Aciclovir by using reverse phase liquid chromatography technique.
3.Also to study the Similarity factor and Difference factor between the two products.

MATRIALS AND METHODS:
DETALS OF PRODUCT-1:
Name of the product: ACYPROVE-200
Batch Number : SPT222460A
Mfg.Date: 10/2022
Exp.Date: 09/2024
Label Claim: Each tablets contains: Aciclovir 200 mg

DETALS OF PRODUCT-2:
Name of the product: ZOVIRAX TABLETS
Batch Number : EN110
Mfg. Date : 05/2023

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Exp. Date : 04/2026
Label Claim : Each tablets contains Aciclovir200mg
ASSAY VALUE OF STANDARD USED:

S.No.	NameoftheStandard	Purity(assuch)
1	Aciclovir	95.31%

CALCULATIONS:

Drug release in mg **:** (SampleArea/StdArea)*(Stdwt./25)*(5/50)*(900/1)*(Purity/100) = mg

Drug release in% **:** (Drug release in mg/Label claiminmg)* 100=%

METHOD OF ANALYSIS:

Dissolution conditions:

DissolutionMedium	:	0.1NHydrochloricacid
Volume	:	900ml
Method	:	Paddle
Speed	:	500RPM
Time	:	30minutes
Temperature	:	37°C±0.5°C.

PROCEDURE:

STANDARD AND SOLUTION:

Weigh 50mg of acyclovir working standard in a 25ml volumetric flask and 0.1N hcl to dissolve and make up the flask upto the mark with same. Further 5ml into 50ml volumetric flask make up to volume with the same.

Sample preparation:

Place 900ml of Medium at 37°C±0.5°Cin 12 dissolution vessels separately and fix in the tablet dissolution bath maintained at 370C ±0.50C. Fix the paddle to the shaft and bringit into the position. Place one tablet each in to 12 dissolution vessels and operate the instrument at 50 RPM for 30 minutes. At the end of 30 minutes, reject first 20ml from the vessels and filter the solution for use.

Mobile phase preparation:

Prepare a mixture of 0.25% Formic acid . Mix well and filter through a Nylon membrane filter paper.

Chromatographic conditions:

Column	:	50mmx4.6mmx3.5µm,C18Inertsil
Injection Volume	:	20µl
Wavelength	:	254nm
Run time	:	3Minutes
Flow	:	1ml/min
Temperature	:	Ambient
Diluents	:	Disso medium

DISSOLUTION CONDITIONS:

Dissolution medium 1: Acidic medium

Medium: 900 ml of 0.1N Hydrochloric Acid
Media Preparation: 102 ml of Hydrochloric acid made upto12 lit with water
Type: Paddle
RPM : 50
Time: 10minutes,15minutes&30minutes.

Dissolution medium 2: Buffer pH6.8

Medium: 900 ml of Phosphate BufferpH6.8
Media Preparation: 6.8g of potassium dihydrogenor thophosphate and 0.88g of sodium Hydroxide transfer into 100 ml of waterand the pH must 6.8 (If necessary, adjust the pH)
Type : Paddle
RPM : 5
Study Timings : 10 minutes, 15 minutes & 30 minutes

Dissolutionmedium3:BufferpH4.5

Medium : 900 mlofAcetateBufferpH4.5
Media preparation: 2.99g of sodium acetate in 800ml of water and adjust the pH: 4.5 with glacial acetic acid. Makeupto1000mlwith water.
Type : Paddle
RPM : 50
Study Timing:10minutes,15minutes&30minutes

Dissolutionmedium3:BufferpH4.5

Medium: 900 mlofAcetateBufferpH4.5
Medium preparation: 2.99g of sodium acetate in 800ml of water and adjust the Ph 4.5 with glacial acetic acid. Makeupto1000mlwith water.
Type: Paddle
RPM : 50
Time: 10minutes, 15minutes&30minutes.

RESULTS AND DISCUSSION

DISSOLUTION RATE IN ACIDIC MEDIUM (0.1NHCL):

Medium : 900ml of 0.1N HCL
Method :Paddle
RPM : 50
Time :10minutes,15minutes &30minutes.

Comparative Dissolution Results:

RELEASEPERCENTAGE

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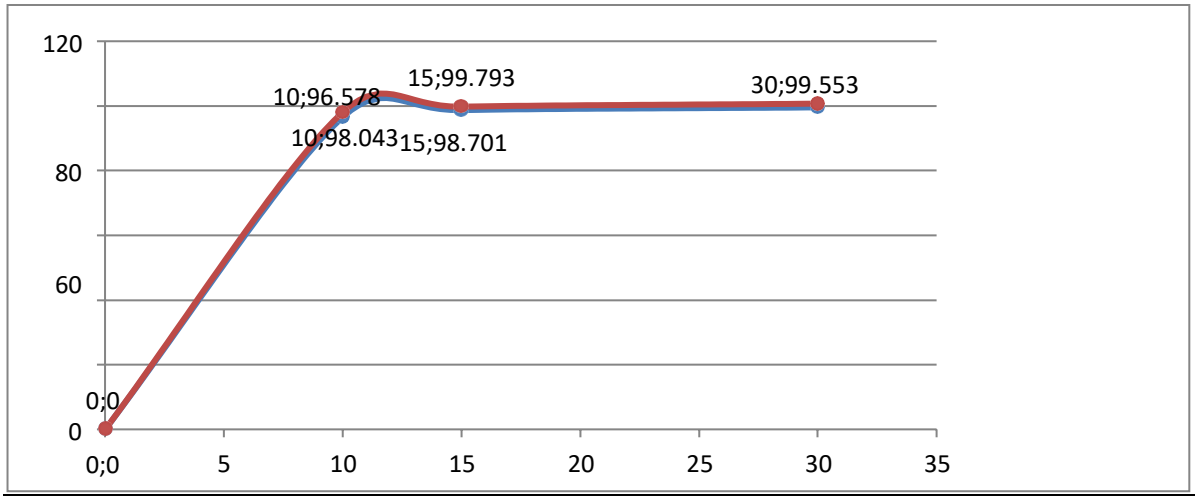
Product Details:	*PRODUCT-1*			*PRODUCT-2*		
Time(inMin):	**10**	**15**	**30**	**10**	**15**	**30**
Vessel-01	97.47	97.81	98.98	98.48	99.50	100.68
Vessel-02	96.76	98.41	99.91	97.80	98.91	100.44
Vessel-03	96.47	98.96	100.16	97.66	99.55	100.23
Vessel-04	97.42	99.37	99.60	98.09	99.92	101.10
Vessel-05	95.96	98.13	98.66	97.38	98.22	101.11
Vessel-06	95.25	98.20	99.67	97.60	99.25	100.71
Vessel-07	97.64	99.45	99.92	98.61	99.91	100.27
Vessel-08	97.01	99.31	100.34	98.50	100.59	100.60
Vessel-09	96.15	99.74	99.75	97.32	100.56	100.62
Vessel-10	96.41	98.34	99.31	98.77	100.65	100.70
Vessel-11	95.27	98.15	99.67	99.08	100.64	101.27
Vessel-12	97.12	98.54	98.67	97.23	99.81	100.67
AVERAGE:	**96.578**	**98.701**	**99.553**	**98.043**	**99.793**	**100.700**
SD:	0.81	0.64	0.55	0.63	0.76	0.32
%RSD:	**0.84**	**0.65**	**0.55**	**0.64**	**0.76**	**0.32**



DIFFERENCE FACTOR CALCULATION:(f1):0-15

Σt=1n|Rt-Tt|= 3.70 **Thereforef2=** **89.83**

[Σt=1nRt]= 298.54

Thereforef1=

SIMILARITY FACTOR CALCULATION :(f2):50-100

n=	3
Σt=1n(Rt-Tt)²=	4.65
(1/n)Σt=1n(Rt-Tt)²=	1.55
1+(1/n)Σt=1n(Rt-Tt)²=	2.55
[1+(1/n)Σt=1n(Rt-Tt)²]⁻⁰˙⁷=	1.60
log[100/1+(1/n)Σt=1n(Rt-Tt)²]⁻⁰˙⁷=	1.797

1.24 DISSOLUTION RATE IN PHOSPHATE BUFFER pH 6.8:

Medium : 900ml of Phosphate buffer pH 6.8
Method : Paddle
RPM :50
Time :10minutes,15minutes &30minutes.

Comparative Dissolution Results:

RELEASEPERCENTAGE

ProductDetails :	*PRODUCT-01*			*PRODUCT-02*		
Time(inMin):	**10**	**15**	**30**	**10**	**15**	**30**
Vessel-01	79.27	91.03	98.51	84.82	95.87	101.63
Vessel-02	73.86	86.07	96.95	88.58	89.39	99.23

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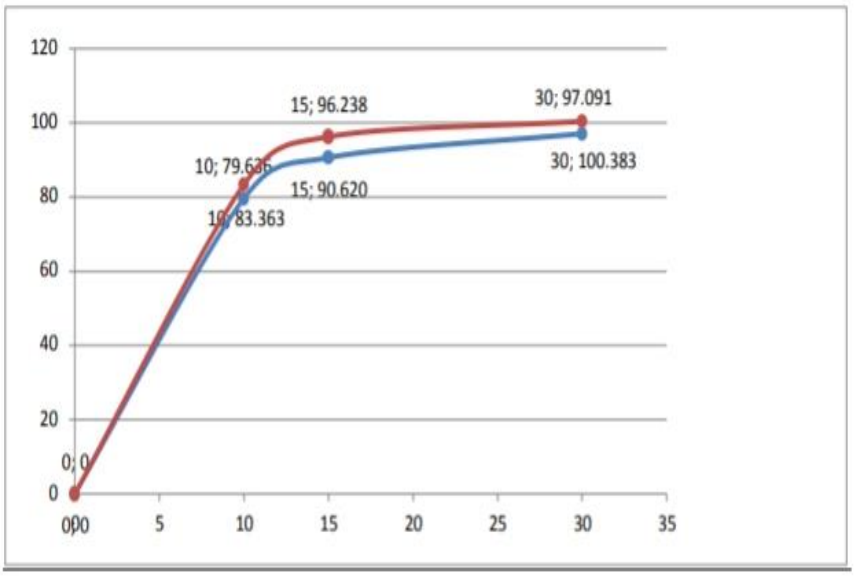
Vessel-03	63.95	87.81	97.06	88.58	89.87	100.22
Vessel-04	80.12	88.73	97.02	79.05	88.36	98.84
Vessel-05	81.62	86.08	95.76	76.66	87.78	97.86
Vessel-06	75.66	80.89	96.39	76.65	86.40	100.95
Vessel-07	82.87	88.69	93.31	80.11	89.93	100.89
Vessel-08	82.42	87.18	99.07	77.31	88.48	99.48
Vessel-09	86.43	89.58	96.60	86.44	89.66	100.82
Vessel-10	81.26	87.63	98.24	81.28	90.42	99.54
Vessel-11	84.39	85.83	95.74	76.13	87.11	98.27
Vessel-12	75.26	88.79	96.24	76.05	89.14	100.34
AVERAGE:	**78.926**	**87.359**	**96.741**	**80.972**	**89.368**	**99.839**
SD:	6.05	2.56	1.51	4.89	2.38	1.16
%RSD:	**7.67**	**2.93**	**1.56**	**6.04**	**2.66**	**1.16**



DIFFERENCEFACTORCALCULATION:(f1):0-15

Σt=1n|Rt-Tt|=	7.15
[Σt=1nRt]=	270.18
Thereforef1=	**2.65**

SIMILARITYFACTORCALCULATION :(f2):50-100

n=	3
(1/n)Σt=1n(Rt-Tt)²=	5.94
1+(1/n)Σt=1n(Rt-Tt)²=	6.94
[1+(1/n)Σt=1n(Rt-Tt)²]⁻º˙7=	2.63
log[100/1+(1/n)Σt=1n(Rt-Tt)²]⁻º˙7=	1.579
Thereforef2=	**78.97**

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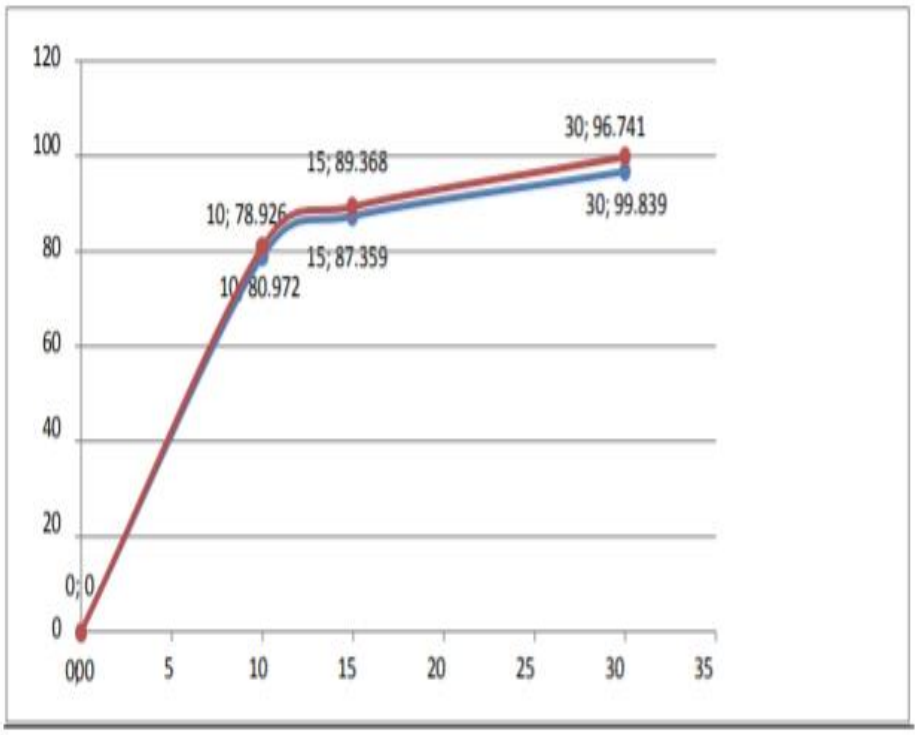
DISSOLUTION RATE IN ACETATE BUFFER pH 4.5:

Medium: 900ml of Acetate buffer pH 4.5
Method : Paddle
RPM : 50
Time :10 minutes,15minutes &30minutes.

Comparative Dissolution Results:
RELEASE PERCENTAGE

ProductDetails:	***PRODUCT-01***			***PRODUCT-02***		
Time(inMin):	**10**	**15**	**30**	**10**	**15**	**30**
Vessel-01	73.55	81.28	96.70	83.45	100.85	101.14
Vessel-02	72.18	81.33	89.90	83.87	91.77	100.67
Vessel-03	88.27	89.31	100.26	79.92	97.62	101.10
Vessel-04	90.51	99.34	99.87	87.49	97.13	99.63
Vessel-05	81.21	96.32	98.61	84.44	97.84	100.03
Vessel-06	78.42	86.94	90.97	81.13	94.63	100.28
Vessel-07	101.48	102.67	103.53	81.69	94.11	99.38
Vessel-08	77.80	101.76	102.59	81.56	93.60	100.30
Vessel-09	69.50	93.98	98.40	82.27	96.43	100.73
Vessel-10	73.78	87.69	98.77	84.43	99.67	101.48
Vessel-11	69.71	85.05	97.28	86.35	97.53	100.31
Vessel-12	79.22	81.77	88.21	83.76	93.68	99.54
AVERAGE:	**79.636**	**90.620**	**97.091**	**83.363**	**96.238**	**100.383**
SD:	9.56	7.95	4.90	2.19	2.71	0.67
%RSD:	**12.00**	**8.77**	**5.05**	**2.63**	**2.82**	**0.67**



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DIFFERENCE FACTOR CALCULATION:(f1):0 -15

$\Sigma t=1n\|Rt-Tt\|=$	12.64
$[\Sigma t=1nRt]=$	279.98
Therefore f1=	**4.51**

SIMILARITY FACTOR CALCULATION:(f2):50–100

n=	3
$\Sigma t=1n(Rt-Tt)^2=$	56.29
$(1/n)\Sigma t=1n(Rt-Tt)^2=$	18.76
$1+(1/n)\Sigma t=1n(Rt-Tt)^2=$	19.76
$[1+(1/n)\Sigma t=1n(Rt-Tt)^2]^{-0.7}=$	4.45
$\log[100/1+(1/n)\Sigma t=1n(Rt-Tt)^2]^{-0.7}=$	1.352
Therefore f2=	**67.60**

SUMMARY AND CONCLUSION:

The curve of Aciclovir in product "ACYPROVE-200[Aciclovir Tablet IP 200MG]" is equivalent to the curve of Aciclovir in product "ZOVIRAX

TABLETS[Aciclovir Tablet IP 200MG]" and was considered similar for following reasons

The Dissolution profile in Acid medium – 0.1 N HCL[Official]

1. The difference factor (f1) is 1.24 which is with in the limit of 0-15
2. The similarity factor (f2) is 89.83 which is also within the limit of 50-100

The Dissolution profile in pH 6.8 buffer medium

1. The difference factor (f1) is 2.65 which is with in the limit of 0-15
2. The similarity factor (f2) is 78.97 which is also within the limit of 50-100

The Dissolution profile in pH 4.5 buffer medium

1. The difference factor (f1) is 4.51 which is with in the limit of 0-15
2. The similarity factor (f2) is 67.60 which is also within the limit of 50-10

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