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# FORMULATION AND EVALUATION OF MICROSPHERE EPIVIR (TABLET) IN HIV DISEASE

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**ABSTRACT**
**OBJECTIVE:** The Epivir controlled-release tablets manufactured in several combinations utilising a direct compression procedure with variable amounts of Carboplol974P and Xanthan gumps. The amount and concentration of RRDs, Carboplol974P and Xanthan gum needed for the desired release of the drug were chosen as independent factors x1 and x2; while the 10% drug-dissolution time required was 10%, t50% to75%, t90%, dependent variables picked
**METHODS**:
**RESULT**: Nine formulations for hardness, friction, thickness, percentage of medication, in-vitro release were created and analysed. The results show that all pharmacopeia-limited formulations and all formules with in vitro dissolution profiles have been match the model of kinetic computing statistical parameter such as intercept (a), slope (b) and regression coefficient (r). equation like Polynomial for T10 percent, T50 percent, T75 percent, T90 percent determined.
**CONCULSION:**
Here more over similar formulation (f2=85.04& No more differential t=0.2005) according to the SUPAC guidelines is the formula including a combination of 10 percent Carboplol974P and 10 percent gum Xanthan (FDK5) (Lamivir). formulation selected on (FDK5) based on Higuchi's kinetics and the drug-release mechanism established as a case- II or a standard Zero release (Non-Fickian, n = 0.915).

## INTRODUCTION

The most convenient use of oral administration is the most popular formulations on the market for both classic and novel medication delivery techniques. Both patients and doctors pick tables. There are numerous obvious reasons, including patient acceptance and simple administration. Conventional formulations for chronic illnesses must submitted at multiple dosage levels in long-term therapy and hence have several disadvantages. Long-term release methods can also seen as attempts at sustainable release. Sustainable release pill allows the medical frequency to be 2 folded or lower than the conventional dosage frequency. Summit . By improving pharmacology and pharmacokinetics, sustainable release products provide a benefit over standard dosage form. There are promising future sustainable releases in some sectors, such as chronopharmacokinetic systems. Customised drug delivery systems, mucoadhesive systems and a good and acceptable particulate system. The development of orally regulated releases of highly water-soluble medications with consistent releases has become a concern for pharmaceutical technologists.

Fast release medicines usually cause toxicity if not prepared for an extended dosage. In the previous year, it was essential to amend and evaluate the condition of HIV therapy that we could not predict. There were new scientific results on the effectiveness, safety and administration of the most contemporary schemes required for this intervention. Management of the 2019 Coronavirus Disease HIV pandemic (COVID-19) has further highlighted some critical issues (and opportunities) that have developed independently from COVID-19 (although increased by the presence of it), both for those facing its initial therapeutic line and for those already effectively suppressed by viro. The COVID-19 epidemic generates a need to change our traditional CART standards so that patient visits for diagnosis, medications and tests may streamlined. necessitated adopting a simple and well-tolerated system with substantial resistance barriers and excellent efficiency[1]. In the case of the genotypical test to identify antirretroviral resistance in clinical practise for assessment of cd4, this highlighted how to preserve the diagnostic algorithm. Despite international progress in HIV prevention and AIDS treatment, HIV infection remains a severe problem in emerging countries. Of around 1.8 million 7 [1.3 million - 2.2 million] children living with HIV, 88% live in sub-Saharan Africa and 53% get treatment by the end of 2019. In 2019, an estimated 95,000 children under 15 globally died of AIDS (8). Without HIV medication, 50% of HIV infected toddlers would die at the age of 2 and children would be more likely to acquire AIDS than adults. The early commencement of antiretroviral therapy for

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infected children brings unquestioned therapeutic benefits by decreasing the probability of premature childhood death (12). If available, ABC/3TC/LPV/r granules are recommended for use in children weighting 3 kilogrammes or more which allow early start of ART in newborns with HIV-1 and therefore assist minimise mortality and morbidity HIV and AIDS. The recipe is masked and has a strawberry aroma, allows a simple dosage of caretakers and aids children to swallow who cannot consume tablets or who have difficulties with conventional LPV/r pellet formulations. As a new single-pill solution, the FDA authorised DTG/3TC 2DR on August 2020 for patients wishing to replace the existing therapy with a fully substituted HIV that provides silent anamnesis or detection of DTG or 3TC RAMs for failure to prevent treatment.

## MATERIAL AND METHODS

The materials utilised collected from several sources in this investigation. Epivir was a cayman chemical pvt.ltd gift sample Carbopol974P and Xanthan gum have obtained from Delhi Other Excipients like aerosil and magnesium stearate from jai bharat gum and chemical pvt.ltd were obtained

## FORMULATION DEVELOPMENT OF EPIVIR SUSTAINED RELEASE TABLETS

The factorial design is a technique for identifying and analysing the process components. You may also find any interaction between the selected items. The factory design includes the selection of parameters and the selection of responses. 26 The proportion of epivir controlled release (CR) tablets used to formulate indigenous variables HPMC Carbopol974P and Xanthan gum explained by a determined level of three two-factor experimentally designed variables (33 factorial designs). The time required determined as depending factors for 10 percent (t10 percent), 50 percent (t50 percent), 75 percent (t75 percent), and 90 percent (t90 percent) of the drug disintegration. Significant terms picked with a trust interval of 95% (p t50 percent), t75%, t90% (step-wise backward Linear Regression Analysis). The three X1 factor levels (Carbopol974P) at a concentration of 5%, 10%, 15%. Three X2 (Xanthan Gum) factor levels utilised as the foundation for the epivir CR formulation design at 5%, 10%, and 15% (percent relative to the entire tablet weight). Total nine epivir control tablet formulations, i.e. X1, X2, and 32 Factorial, are created using selected combinations. The importance of the combined effects of X1, X2, have been examined to identify the optimal combination and concentration to achieve long-dose dosage release.

## PREPARATION OF EPIVIR CONTROLLED RELEASE TABLETS

All components have precisely gathered and weighed. Sift Epivir USP by sieve No. 60# with avicel PH 102, and rinse with other excipients. Separately tap colloid silicone dioxide (aerosil-200) and magnesium stearate through seve no. 60#. Pre-blend for 15 minutes in blender all components (excluding lubricantmagnesium stearate). Magnesium stearate is added and then 5-6 minutes mix again. Using rotative tablet punching machine (RIMEK), Ahmedabad, lubricated powder is crushed. Compressed pills were evaluated under official norms and unauthorised testing. Tablets packed in well-closed resistance to light and humidity resistant containers

## EXPERIMENTAL DESIGN

The experimental design employed in this research adopted X1 and Xanthan Gum concentration as X2 to optimise concentration of polymers like Carbopol974P concentration. The experimental design shown in Table 1. Three levels were selected and classed as -1= 5%, 0=10%, +1=15%. Formulae provided in Table 2 for all experimental batches

**TABLE 1: LAYOUT DESIGN OF EXPERIMENTAL**

| Formulation | X1 | X2 |
|---|---|---|
| **FD1** | **1** | 1 |
| **FD2** | **1** | 0 |
| **FD3** | **1** | -1 |
| **FD4** | **0** | 1 |
| **FD5** | **0** | 0 |
| **FD6** | **0** | -1 |
| **FD7** | **-1** | 1 |
| **FD8** | -1 | 0 |
| **FD9** | -1 | -1 |

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**TABLE 2: FORMULA FOR THE PREPARAING OF EPIVIR SUSTAINED RELEASE TABLETS AS PER EXPEROMENTAL DESIGN**

| Name of Ingredients | Quantity of Ingredients per each Tablet (mg) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | $F_1$ | $F_2$ | $F_3$ | $F_4$ | $F_5$ | $F_6$ | $F_7$ | $F_8$ | $F_9$ |
| Lamivudine | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 |
| Avicel PH 102 | 120 | 140 | 160 | 140 | 160 | 180 | 160 | 180 | 200 |
| Carbopol974P | 60 | 60 | 60 | 40 | 40 | 40 | 20 | 20 | 20 |
| Xanthan Gum | 60 | 40 | 20 | 60 | 40 | 20 | 60 | 40 | 20 |
| Aerosil | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Magnesium Stearate | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Total Weight | 400 | 400 | 400 | 400 | 400 | 400 | 400 | 400 | 400 |

**EVALUATION OF EPIVIR CONTROLLED RELEASE TABLETS**

**HARDNESS**

Diametric tablet compression was assessed using a Monsanto Hardness Tester. A tablet hardness of about 2-4 kg/cm2 is considered to be appropriate mechanical stability.

**FRIABILITY**

The friability of the tablets was evaluated in a Roche friabilator (Camp-bell Electronics, Mumbai). For a set time in a drum the tablets with the known weight (W0) or sample 20 tablets are again dusted and weighed (W) (100 revolutions). The weight decrease as stated in the following calculation determined the fragility of the %. The weight reduction should not exceed 1%.

**FRIABILITY (%) = [(INITIAL WEIGHT- FINAL WEIGHT)]/ INITIAL WEIGHT X 100**

**CONTENT UNIFORMITY**

The test chose 20 pills alone and estimated the medicines and tablets percentage, not less than 85% or more, of the labelled pharmaceuticals content, at the time of the test.

**ASSAY**

Weighed and sophisticated The pH 6.8 buffer was withdrawn and a carefully weighted powder volume of 100 mg of epivir extracted and 0.45 micronutrient membrane used to filter the solution. Using UV-visible spectrophotometric dilution at 270nm, absorbance was measured.

**THICKNESS**

The thickness of all formulations of tablets was measured using vernier callipers between the two arms of the vernier callipers.

**STUDY OF IN- VITRO DISSOLUTION**

The in vitro dissolution test for the release epivir-controlled tablets was done with the dissolution medium paddle type 900 ml of the 0.1 N HCl for 2 hours, followed by the phosphate buffer pH 6.8 at 50 rpm for next 10 hours, and by the dissolution testing device USP XXIII Type II temperature 37±0.5°C. Five ml of the samples were collected using a filter-equipped syringe and the volume withdrawn was replaced by the same quantity of new dissolving medium at the interval. The findings assessed by measuring UV visible spectrophotometer absorption at 270 nm after sufficient dilutions for the presence of drug release. Decisions have been taken three times (n=3).

**MODELING OF KINETIC DRUG RELEASE**

To prove the kinetic modelling of the release of drugs, all formulations have been dissolved in zero order first order, Higuchi and Korsmeyer-Pepa models.

**RESULT AND DISCUSSION**

The controlled release consists of 32 factorial designs to ensure the selection of the best combination of CARBOPOL974P, XANTHAN GUM, and long-term / long-term dose release of the medicine. The two key

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elements involved in formulations are concentration of CARBOPOL974P and XANTHAN GUM polymers as independent variables (X1, X2) and in vitro dissolution characteristics (t10%). All 150 mg of epivir formulations were manufactured as controlled release tablets using three levels of 2 factors and the Direct Compression technique as per the formulae provided in Table 2. Table 3 investigated the different post-compression properties of all manufactured tablets, their drug content, mean hardening, friability, average thickness, and the finding according to the allowed procedure. The tablet durability ranged from 4.78 to 6.35 kg/cm2. The weight loss of friability tests was less than 0.52 percent. The drug content of the tablets manufactured was satisfactory. In-vitro Dissolution experiments have been performed on prepared tables using a medium of 0,1 N HCl for first 2 hours, followed by a phosphate buffer of 6,8 hours for 10 hours at 50 rpm and a temperature of 37 ± 0.5 °C during remaining 10 hours. The dissolving profiles are shown in Fig.1 and the dissolution parameters in Table 5.A large variation found in t10%, t50%, t75% and t90% due to wording issues. Forms F5 containing 40 mg CARBOPOL974P 40 mg XANTHAN GUM showed promising dissolving characteristics (t10% = 0.428h, t50% = 2.816h, t75% = 5.633 h, t90% = 9.359h). The variation in the starting time burst effect is related to the variable in the viscosity of the polymer mixture. Dortunc and Gunal noted that increased viscosity led to a corresponding decline in drug releases that might be associated with the thicker gel layer composition.

**TABLE 3: POST EXPRESSION PARAMETERS FOR THE FORMULATION**

| FORMULATION | HARDNESS | DIAMETER | THICKNESS | FRIABILITY | DRUGCONTENT |
|---|---|---|---|---|---|
| FD1 | 4.78 | 9.51 | 4.81 | 0.467 | 94.79 ± 1.31 |
| FD2 | 5.65 | 9.50 | 5.220 | 0.473 | 97.41 ±1.12 |
| FD3 | 5.05 | 9.51 | 4.85 | 0.353 | 97.30 ± 1.0 |
| FD4 | 4.85 | 9.50 | 5.03 | 0.414 | 96.35 ± 1.46 |
| FD5 | 5.95 | 9.50 | 5.47 | 0.409 | 99.25 ± 1.15 |
| FD6 | 6.35 | 9.51 | 5.18 | 0.338 | 99.81 ± 1.13 |
| FD7 | 6.15 | 9.50 | 5.17 | 0.340 | 99.30 ± 1.0 |
| FD8 | 5.35 | 9.50 | 5.01 | 0.358 | 97.19 ±1.31 |
| FD9 | 5.05 | 9.51 | 5.00 | 0.359 | 95.64 ± 1.64 |

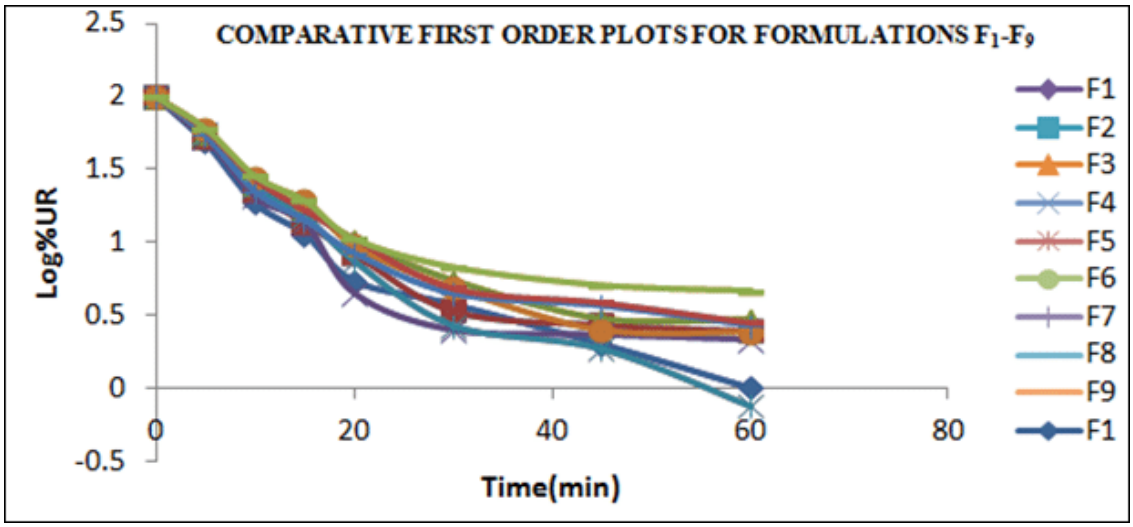


**FIG 1: COMPERATIVE ZERO ORDER PLOTS F1-F9**

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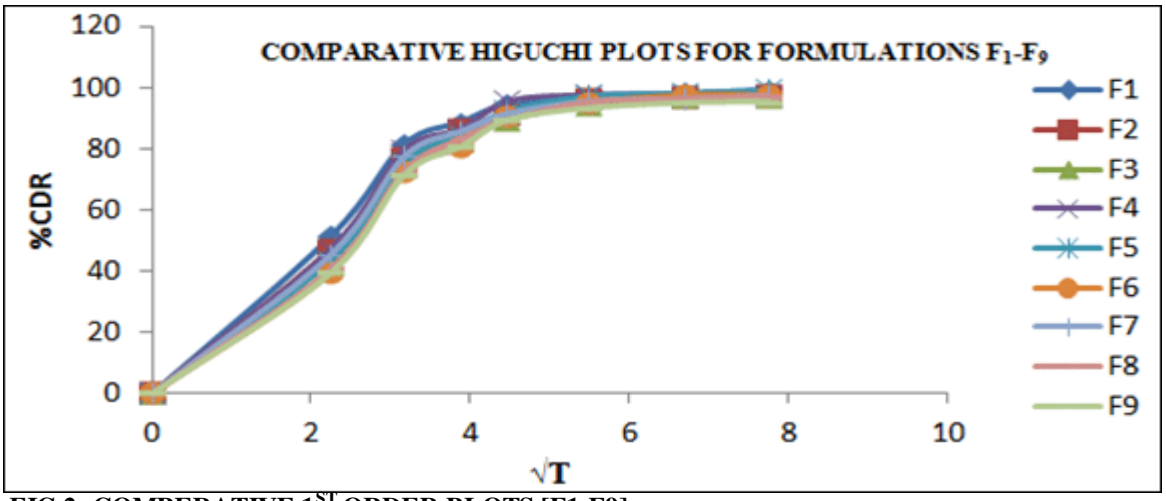


FIG 2: COMPERATIVE 1ST ORDER PLOTS [F1-F9]

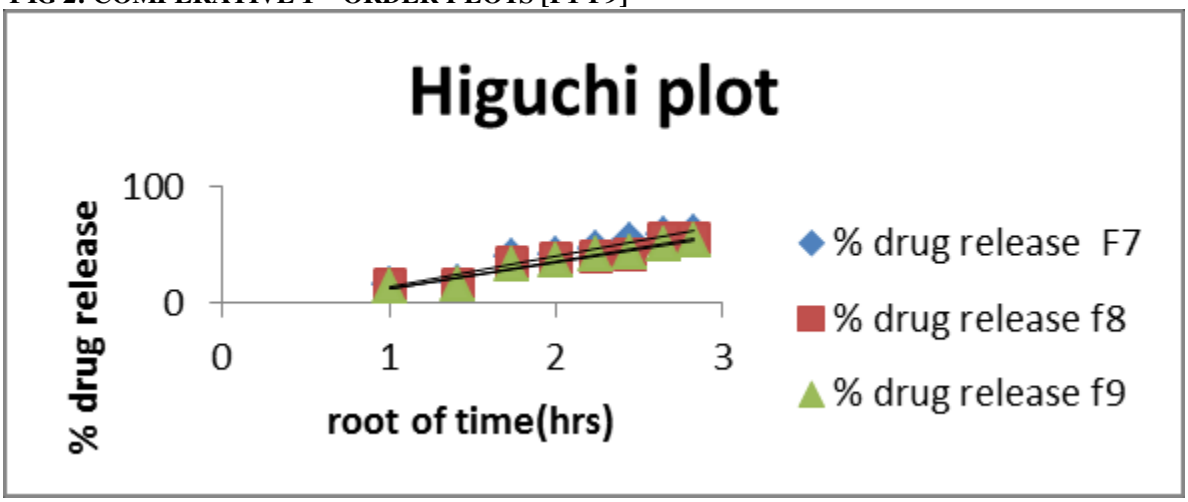


FIG 3: COMPARATIVE HIGUCHI PLOT [F1-F9]

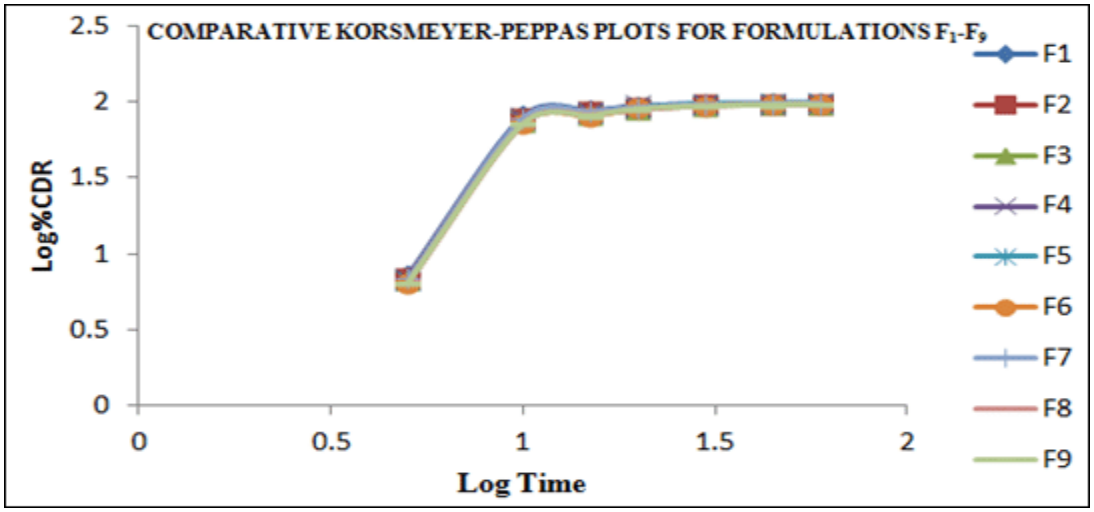


FIG 4: COMPARATIVE KORESMEYER PEPPAS PLOT FOR FORMULATION

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first examined in-vitro under the zero-order linear regression analysis and the kinetic equations of Higuchi and Korsmeyer-Peppas to evaluate the mechanism of drug release. The results of the linear regression research, including regression coefficients, are described in Table 4 and Fig. 1-4. The dissolution of all tablets with determination coefficient (R2) over 0.984 found from above.

**TABLE4: REGRESSION ANALYSIS DATA OF 32 FACTORIAL DESIGN FORMULATION OF EPIVIR**

| | Formulation Code | Kinetic Parameters | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Zero Order | | | First Order | | | Higuchi | | | Korsmeyer-Peppas | | |
| S.No | | a | b | r | a | b | r | a | b | r | a | b | r |
| 1 | $F_1$ | 9.22 | 7.02 | 0.99 | 2.08 | 0.08 | 0.95 | 8.64 | 26.65 | 0.97 | 1.01 | 0.90 | 0.96 |
| 2 | $F_2$ | 10.34 | 7.06 | 0.99 | 2.08 | 0.08 | 0.95 | 7.85 | 26.90 | 0.97 | 1.02 | 0.90 | 0.96 |
| 3 | $F_3$ | 5.07 | 6.88 | 0.99 | 2.06 | 0.07 | 0.97 | 12.08 | 25.98 | 0.97 | 0.87 | 1.02 | 0.98 |
| 4 | $F_4$ | 9.12 | 7.19 | 0.99 | 2.12 | 0.09 | 0.91 | 8.99 | 27.23 | 0.97 | 1.01 | 0.92 | 0.96 |
| 5 | $F_5$ | 10.14 | 7.27 | 0.99 | 2.16 | 0.11 | 0.88 | 8.34 | 27.59 | 0.97 | 1.02 | 0.92 | 0.96 |
| 6 | $F_6$ | 10.28 | 7.20 | 0.98 | 2.10 | 0.09 | 0.91 | 9.00 | 27.76 | 0.98 | 0.94 | 1.01 | 0.96 |
| 7 | $F_7$ | 6.29 | 6.91 | 0.99 | 2.06 | 0.07 | 0.97 | 11.16 | 26.19 | 0.97 | 0.90 | 1.00 | 0.98 |
| 8 | $F_8$ | 9.36 | 7.13 | 0.99 | 2.08 | 0.08 | 0.94 | 9.63 | 27.44 | 0.98 | 0.92 | 1.02 | 0.96 |
| 9 | $F_9$ | 4.21 | 7.36 | 0.99 | 2.14 | 0.09 | 0.89 | 13.16 | 27.34 | 0.95 | 0.91 | 0.98 | 0.98 |
| 10 | IP | 3.08 | 8.10 | 1.00 | 2.27 | 0.13 | 0.84 | 16.11 | 30.15 | 0.96 | 0.88 | 1.06 | 0.99 |

The r values of Higuchi's factory formulations were found to be within the range 0.953–0.983 and indicate that the data were well-compared with the time equation Higuchi square root, which validated the release followed by the diffusion process. Slope(n) values vary from the 0.873- polynomial equation in Equation Y=b0+b1 X1+b2 X2+b12X12+B11X12+b22X22 to 32 full faktorial design... Kinetic data for the Peppa equation also discussed. Y is a dependent variable, b0 is an arithmetical mean response of 9 lots, and b1 is an estimated factor X1. The main effects (X1 and X2) reflect the average consequence of variations from a low to high value component one at a time. The interaction term (X1X2) shows how the answer changes when two factors simultaneously change. The polynomial terms (X12 and X22) are utilised for non-linearity testing

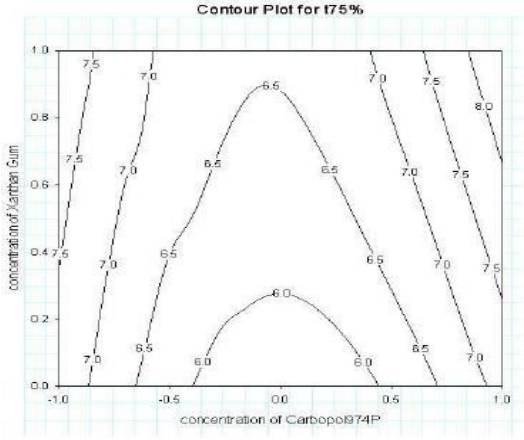


**FIG 5: LINEAR CONTOUR PLOT FOR T 75%**

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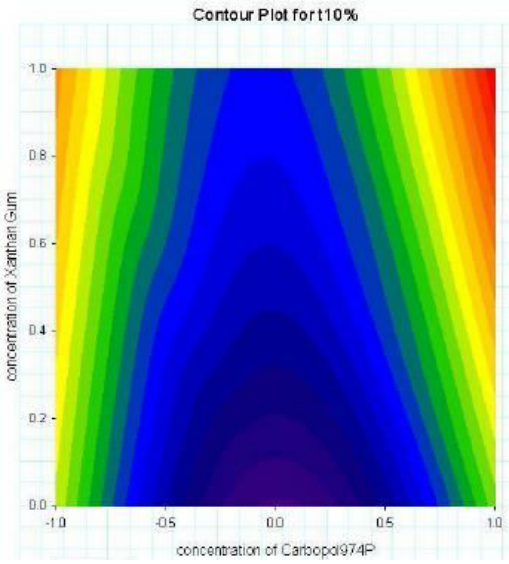


**FIG6: LINEAR CONTOUR PLOT FOR 10%**

**TABLE 5: DISSOLUTION PARAMETERS OF EPIVIR CONTREOLLED RELEASED TABLETS FULL FACTORIAL DESIGN**

| CODE | KINETIC PARAMETERS | | | |
|---|---|---|---|---|
| | T10% | T 50% | T 75% | T90% |
| F1 | 0.572 | 3.764 | 7.529 | 12.509 |
| F2 | 0.545 | 3.584 | 7.167 | 11.908 |
| F3 | 0.705 | 4.638 | 9.297 | 15.411 |
| F4 | 0.490 | 3.247 | 6.457 | 10.758 |
| F5 | 0.428 | 2.816 | 5.633 | 9.359 |
| F6 | 0.505 | 3.322 | 6.645 | 11.040 |
| F7 | 0.678 | 4.457 | 8.945 | 14.812 |
| F8 | 0.557 | 3.662 | 7.345 | 12.169 |
| F9 | 0510 | 3.356 | 6.211 | 11.151 |
| IP | 0.348 | 2.245 | 4.547 | 7.600 |

The equations for t10%, t50%, t75% and t90% have developed as follows. Y1= 0.555+0.013X1+0.003X2-0.075X1X2+0.120 X1 2+0.067X2 2 0.055+0.013X1 +0.002X2-0.0075X2 +0.120 +0.0260X4 2 0.055+0.013X1 +0.002X2-0.075X2 +0.120 +0.1202 (for t10 percent )

Y2= 3.647+0.085X1+0.022X2-0.494 X1X1 &0.789 X1 2&0.44 X2 2 X2= 3.647 +0.085X1+0.022X2-0494 3.647 +0.085X2+0.022X2-05226 +0.0246 +0.065X1 +0.085x2 +0.022X1-0490 (for t50 percent )

Y3= 7.295+0.170X1+0.044X2-0.988X1X2+1.577 X1 2+0.880X2 2 2+0. X1 2+0.880x2 X1 2+0.880x2 X1 2+0. (for t75 percent )

The positive sign for the coefficient of X1 in Y1, Y2, Y3, and Y4 equations shows that the concentration of CARBOPOL 974P rises by 10%, t50%, t75%, t90%. In other words, the results demonstrate that the time needed for releasing the medicine is impacted by both X1 (CARBOPOL974P) and X2 (XANTHAN GUM) (t10 percent , t50 percent , t75 percent and t90 percent ). The results may conclude that an increase in polymer volumes may lead to lower drug release rates, and drug release patterns may be changed by selecting the levels X1 and X2 appropriately.

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The ultimate best (optimised) formulation (F5) shows a similarity factor(f2)85.454 compared to innovative (lamivir), a differential factor(f1) 2.392 (No meaningful release difference as the levels of the tcal are <0.05).

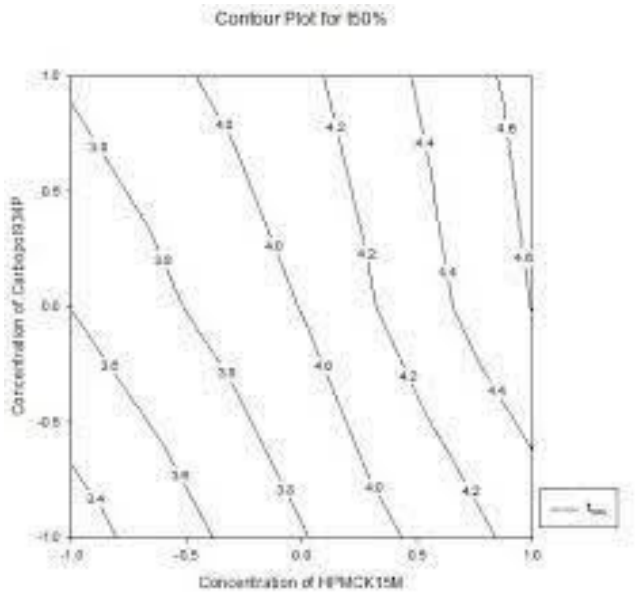


**FIG 7: LINEAR CONTOUR PLOT T50%**

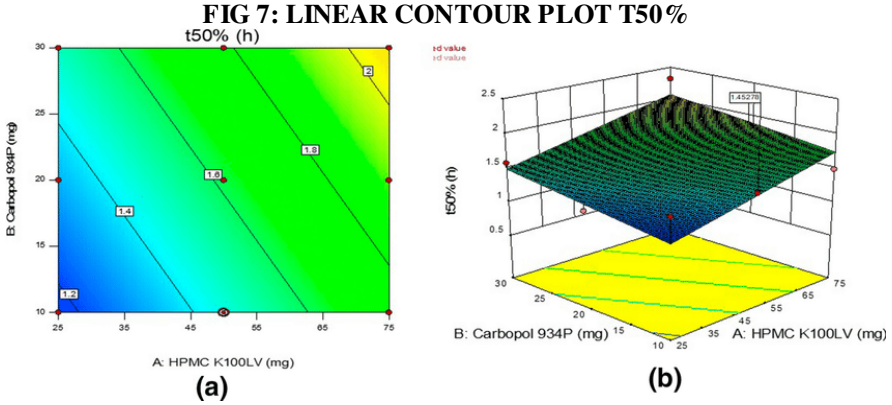


**FIG 8: CONTOUR PLOT T50%**

## CONCLUSIONS

The project is presently examining the utilisation of rating retardants such as Carbopol974P and Xanthan Gum to design and manufacture 32-factorial epivir controlled discharge tablets. It is clear from the results that the drug's release rate is delayed due to the increase in the backward concentration and the combination of the two release retardants cannot used. the medicine does not interact with the drug that can be useful for achieving the desired controlled release over a more extended period. The enhanced formulations followed Higuchi's kinetics. The drug release mechanism established to be non-Fickian transport, Case II or the standard sort of zero order release, governed by the diffusion of swelling matrix. Based on evaluation parameters, the optimum F5 formulation can given once a day for the management of AIDS, other viral diseases.

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