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## RESEARCH ARTICLE

**IN VITRO EVALUATION OF CHEMICALLY DEACETYLATED XANTHAN GUM AS MATRIX POLYMER FOR CONTROLLED RELEASE TABLETS**

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**ABSTRACT**

The objective of the present investigation is to prepare Deacetylated Xanthan Gum, a new Xanthan Gum based polymer and to evaluate its application in controlled release (CR) and in the design of Simvastatin controlled release tablets. Deacetylated Xanthan Gum polymer was prepared by gelatinization of Xanthan Gum in the presence of sodium hydroxide. Matrix tablets each containing 40 mg of Simvastatin were formulated employing Deacetylated Xanthan Gum polymer in different proportions of drug and polymer and the tablets were evaluated. Simvastatin release from the formulated tablets was slow and spread over 12 hr and depended on percent polymer in the tablet. Release was diffusion controlled and followed zero order kinetics. Non – Fickian diffusion was the drug release mechanism from the formulated tablets. Simvastatin release from matrix tablets F1 formulated employing 37 % Deacetylated Xanthan Gum was found suitable for the design of oral controlled release tablets.

**Key-words:** Deacetylated Xanthan Gum, Controlled release, Simvastatin, Matrix tablets.**INTRODUCTION**

In the recent decades, controlled release dosage forms have made significant progress in terms of formulation technology and therapeutic efficacy. Drug release from the formulation should be at a Predictable rate for better patient compliance. Polymers, which are used as release retarding materials in the design of controlled release dosage forms, play an important role in controlling the release of drug from these dosage forms. Though a wide range of polymers and other release retarding polymeric materials are available, there is a need to develop new materials as the newly discovered API's as well as current Drugs are posing a great deal of challenge in formulating safe and effective formulations. Xanthan Gum is a natural, biodegradable polymer and modified Xanthan Gum is reported as fillers<sup>1</sup>, Disintegrants and dry binders. In the present study, a new Xanthan Gum based polymer, Deacetylated Xanthan Gum was synthesized and evaluated for its application in controlled release<sup>2, 3</sup>. Among the various approaches, preparation of matrix tablet is one of the Easiest approaches for obtaining a controlled release. Simvastatin containing matrix tablets were prepared employing Deacetylated Xanthan Gum and evaluated for controlled release. Controlled release formulation is needed for simvastatin because of it is a BCS Class II Drug with low dissolution and high permeability<sup>4</sup>.

**MATERIALS AND METHODS****Materials**

Simvastatin is a gift sample from M/s. Dr. Reddy's Labs Pvt. Ltd., Hyderabad. All other materials used were of Pharmacopoeial grade.

**Methods****Preparation of deacetylated xanthan gum**

The reactions for deacetylation of xanthan Gum was carried out with 1% xanthan solutions and sodium hydroxide, in the concentrations 0.01 mol.L<sup>-1</sup>. An Erlenmeyer flask (240 ml) containing 125 ml of the above solution is incubated in an orbital shaker at 300 RPM. The reaction was pre-set a time of 3 hours and a temperature of 25 °C. The solutions were neutralized with hydrochloric acid (2mol.l<sup>-1</sup>). The biopolymer was recovered by precipitation with ethanol, dried in an oven at 56 °C, until reaching a constant weight and then milled with a disc mill to a particle size of 0.5 mm.

**Preparation of tablets**

Matrix tablets each containing 40 mg of Simvastatin were prepared employing Deacetylated Xanthan Gum in different proportions of drug and polymer. The required quantities of Simvastatin and matrix materials were mixed thoroughly in a mortar by following geometric dilution technique. The binder solution (5% starch) was added and mixed thoroughly to form wet mass. The mass was passed through mesh No. 12 to obtain wet granules. The wet granules were dried at 56° for 4 h. The dried granules were passed through mesh No. 16 to break the aggregates. The lubricants talc (5mg) and magnesium stearate (5mg) were passed

through mesh No. 100 onto dry granules and blended in a closed polyethylene bag. The tablet granules were compressed into tablets on a rotary multi-station tablet punching machine (Simach Machinery Co. Pvt. Ltd.,

Mumbai) with a hardness of 6 - 8kg/sq.cm. Using 9 mm round and Concave punches. Hardness of tablets was tested using a Monsanto hardness tester. Friability of tablets was determined in a Roche Friabilator.

**Table 1: Composition of Deacetylated Xanthan Gum based controlled release tablets of Simvastatin**

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Simvastatin	40	40	40	40	40	40	40	40	40
Deacetylated Xanthan gum	130	120	110	100	80	60	40	20	00
Lactose	70	75	75	80	85	90	95	100	105
Starch	20	25	25	30	35	40	45	40	55
MCC	40	40	45	45	40	55	60	65	70
PVP-K30	40	40	45	45	40	55	60	65	70
Magnesium stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5

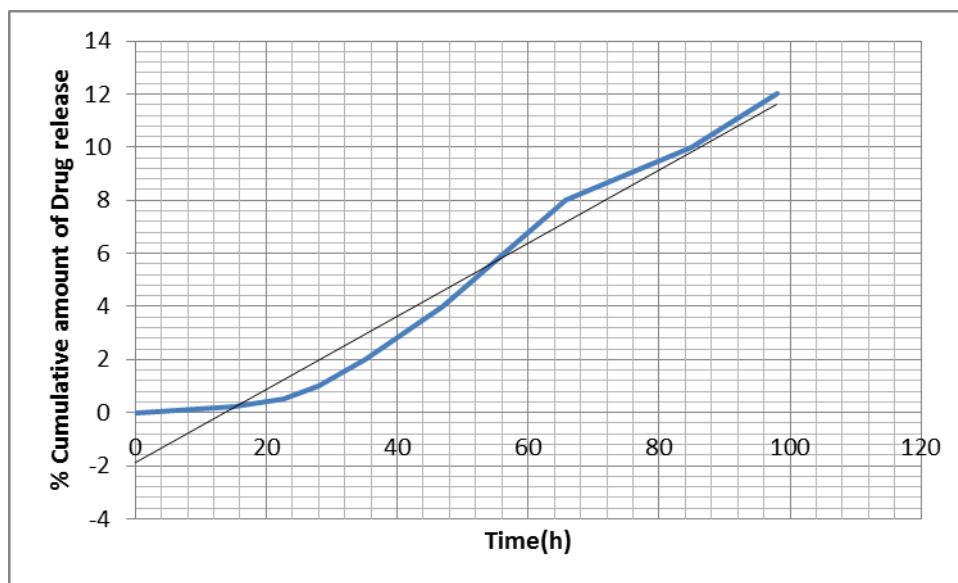
### In vitro dissolution studies

Simvastatin content of the tablets was estimated by UV-Visible spectrophotometric method based on the measurement of absorbance at 238 nm in phosphate buffer of pH 7.4. The method obeyed Beer's law in the concentration range 0-10 µg/ml. No interference from the excipients used was observed. Drug release from matrix tablets was studied using 8 station dissolution rate test apparatus (Lab India, Disso 2000) employing a paddle stirrer at 40 RPM and at 37±1°C. Phosphate buffer of pH 7.4 (900 ml) was used as dissolution fluid. Samples of 5 ml of each were withdrawn at different time intervals over a period of 12 h. Each sample withdrawn was replaced with an equal amount of fresh dissolution medium. Samples were suitably diluted and assayed at 238 nm for Simvastatin using a Shimadzu

UV-140 double beam UV-spectrophotometer. The drug release experiments were conducted in triplicate. Results of in-vitro dissolution studies obtained were tabulated and shown graphically according to following models of data treatment<sup>5</sup>.

1. Cumulative Percentage Drug Release V/s Time in Hours.
2. Cumulative Percentage Drug Retained V/s Time in Hours.
3. Higuchi's Classical Diffusion Equation - Cumulative Percentage Drug Release V/s Square Root T.
4. Korsmeyer Peppas Equation – log cumulative % Drug release V/s log Time<sup>7</sup>

## RESULTS AND DISCUSSION



**Figure 1: % Cumulative drug release graph for suitable formulation**

Deacetylated Xanthan Gum was prepared by gelatinizing Xanthan Gum in the presence of sodium hydroxide. The Deacetylated Xanthan Gum polymer formed was found to be dry and free flowing powder. It

was insoluble in water, aqueous fluids of acidic and alkaline pH. When tested for melting point, the polymer charred at 2200 C. Matrix tablets each containing 40 mg of Simvastatin could be prepared employing different

proportions of Deacetylated Xanthan Gum polymer by wet granulation technique. Hardness of the tablets was found to be in the range of 6 – 8 kg/ sq. cm. Weight loss in the friability test was less than 1% in all the batches. All the tablets contained Simvastatin within  $100 \pm 5\%$  of the labeled amount. Tablets have not disintegrated in water and aqueous, acidic (pH 1.2) and alkaline (pH 7.4) fluids. As such, the prepared tablets were of good quality with regard to drug content, hardness and friability. As the tablets formulated employing Deacetylated Xanthan Gum were non-disintegrating in acidic and alkaline fluids, they are considered suitable for oral controlled release. Release parameters of the tablets are summarized in Table 2. Simvastatin release from the prepared tablets was slow and spread over 12 h. and depended on the concentration of Deacetylated Xanthan Gum polymer. When the release data were analyzed as per zero and first order kinetic models, the best fit with higher correlation ( $r^2 > 0.9581$ ) was

observed with zero order models indicating that the drug release from all the tablets followed zero order kinetics. When the release data were analyzed for Peppas equation, the release exponent 'n' was found in the range 0.497 – 0.886 indicating non – Fickian (anomalous) diffusion as the release mechanism from all the tablets prepared. Plots of percent released versus square root of time was found to be linear ( $r > 0.948$ ) with most of the batches of tablets prepared indicating that the drug release from the tablets was diffusion controlled. As the polymer concentration was increased, release rate was decreased. The Good linear relationship was observed between percent polymer and release rate. Thus the drug release from the matrix tablets could be controlled by varying the proportion of drug: polymer in the matrix. Hence, matrix tablets formulated employing Deacetylated Xanthan Gum (F1) is considered suitable for controlling release of Simvastatin over 12 h.

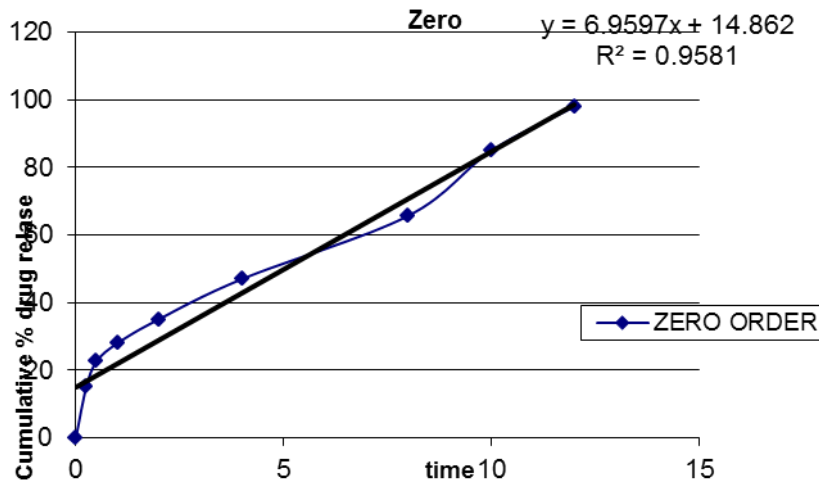


Figure 2: Zero Order release graph for suitable formulation

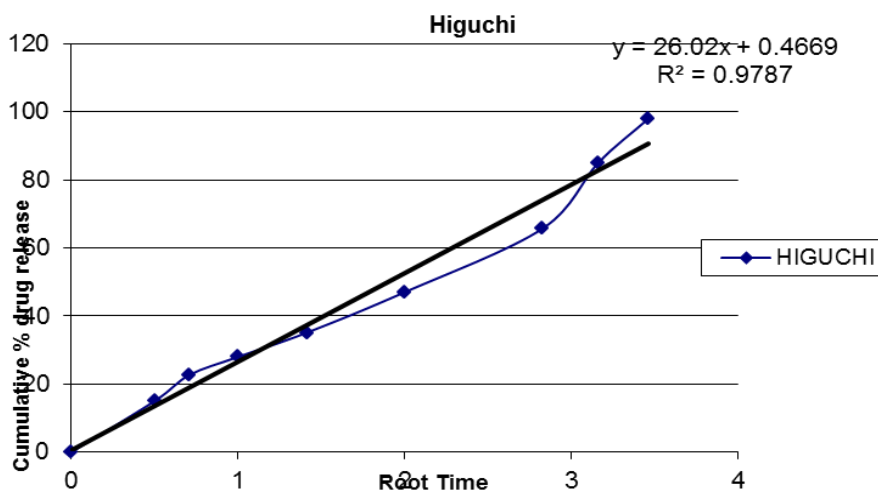


Figure 4: Higuchi's release profile for suitable formulation

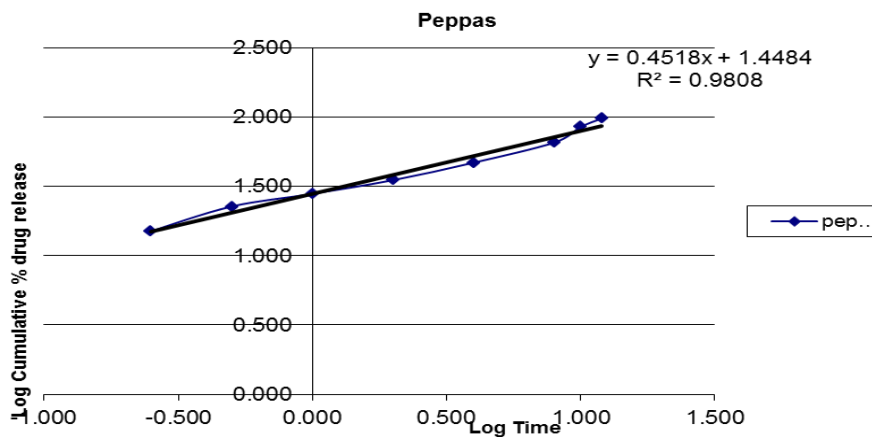


Figure 5: Korsymeyer Peppas release profile for suitable formulation

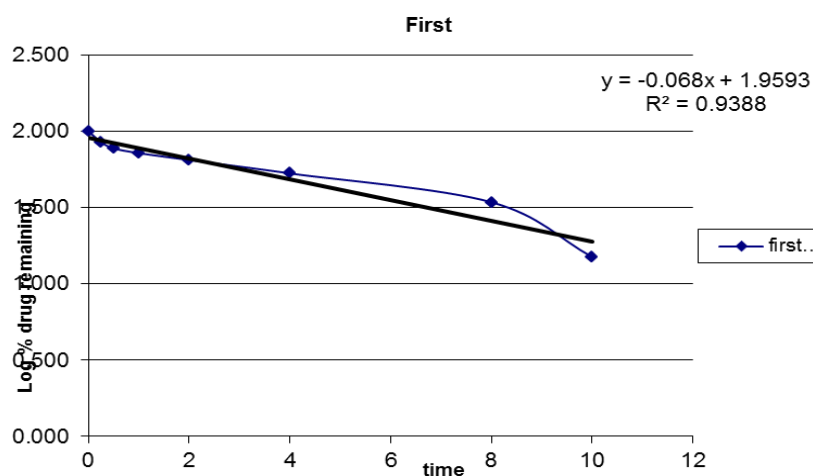


Figure 6: First order release profile for suitable formulation

## CONCLUSIONS

Matrix tablets formulated employing Deacetylated Xanthan Gum, a new Xanthan Gum based polymer, are suitable for oral controlled release of Simvastatin. Drug release from the tablets formulated employing Deacetylated Xanthan Gum was slow and spread over 12 h. and depended on percent polymer in the tablet. Release was diffusion controlled and followed zero order kinetics. Non – Fickian diffusion was the drug release mechanism from the formulated tablets. Simvastatin release from matrix tablets F1 formulated employing 37 % Deacetylated Xanthan Gum polymer is Suitable controlled release formulation. Deacetylated

Xanthan Gum polymer is suitable for the design of oral controlled release tablets.

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## CONFLICT OF INTEREST

We are Glad to disclose we have No Conflict of interest.

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