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Biodegradable Film From Psyllium Seed Husk For Slow Drug Release: *In Vitro* Investigation

Shweta Chouksey, Laxmi Gond
Department of chemistry,
Govt. Science College, Jabalpur, India

Abstract: A biodegradable film was prepared from psyllium seed husk, dimer acid (a dimer of ricinoleic acid derived from castor oil) and polyvinyl alcohol. Film was characterized by FTIR spectroscopy, X-ray diffraction analysis and scanning electron microscopy. Film exhibits optimal mechanical strength with UV protective effect and restricted entry of chemical contaminants. Film can be easily disposed by burying in soil. Films may be a potential eco-friendly food packaging material. Film was loaded with crystal violet and the release data were analysed using zero order, first-order, Higuchi, Hixson–Crowell and Korsmeyer–Peppas kinetic models. Release medium affected the mechanism of drug release. Release medium affected the mechanism of drug release. Release of CV from PDCV perfectly followed Higuchi drug release model. Fickian diffusion was observed at pH 4 and super case-II transport at pH 9. At pH 7, PBS and aqueous medium Fickian diffusion and swelling-induced polymer chain relaxation followed by gel surface erosion was inferred, which accounts for zero-order release. The film conformed to the attributes of a good film dressing.

Index Terms **- Biodegradable film, crystal violet, release kinetics, psyllium seed husk, dimer acid.**

I. INTRODUCTION

Polysaccharides are abundant, biocompatible, biodegradable, nontoxic, non-reactogenic and low-cost biomaterials for development of various drug delivery device. Polysaccharides suffer with certain drawbacks, namely uncontrolled rate of hydration, thickening, drop in viscosity on storage, microbial contamination, thermosensitivity and sensitivity to highly stressful conditions (Setia, 2018). Functional properties of polysaccharides can be improved and modified by the grafting of vinyl monomers (Maji & Maiti, 2021) and crosslinking (Kumar et al., 2017, Rao et al., 2017). Preparation of hydrogels from polysaccharides by network formation controls the polymer-drug interaction, enhances the loading capability and allows to tailor the drug release profile (Barclay et al., 2019, Dubey et al., 2020, Muhamad et al., 2019). Psyllium seed husk (PH) is a natural, fibrous, food grade polysaccharide widely used in medicinal, pharmaceutical and food industry applications (Kamel et al., 2020). Hemicellulose arabinoxylan, a major constituent of PH, has film-forming, swelling, biocompatibility and mechanical properties, hence is a promising candidate for pharmaceutical and biomedical applications. Though, a need for further improvement in the drug delivery and wound healing characteristics was recommended (Ahmad et al., 2021).

In the present study, PSH and dimer acid (DA) were irradiated with microwave, where no organic solvent was used. The product was blended with polyvinyl alcohol (PVA) to prepare a film, PDPV. PVA was selected for blending as it has good film forming tendency in addition to its biocompatibility and biodegradability (Zhang et al., 2012, Hou et al., 2015, Halima & Nihed, 2016). Chemically crosslinked film, PDGL was prepared by blending of PD and PVA in presence of glutaraldehyde. PVDV and PVGL were compared for their performance. PDPV was used to prepare drug loaded films using crystal violet (a cationic dye) as models for study of *in vitro* release profile.

II. MATERIALS AND METHODS

2.1 Materials

PH was purchased from Sidpur Sat Isabgol Factory, Gujarat (India), Dimer acid 1010 (DA) (composition 98% + trimer acid 2%) was supplied by Jayant oil Mills Mumbai (India). Crystal violet (CV) and PVA (Mw 1,15,000) were purchased from Hi Media Laboratories Pvt. Ltd., Mumbai, deionized (DI) water from Millipore water purification system model Elix-3 was used in all the preparations and measurements. All materials and reagents were of standard grade and were used as received.

2.2 Preparation of the film

PH (0.5 g) and DA (0.5 g) were irradiated in a microwave oven to obtain an amorphous mass (PD). PD was mixed with DI water (10 mL) stirred for 30 min, then added 6.7% aq. solution of PVA (3mL), glycerol (1 mL), and DI water (10 mL). This mixture was poured into petri plate and kept in a hot air oven at 60^0C for 6 h to evaporate water. The film thus obtained will be referred as PDPV hereafter.

2.3 Preparation of CV loaded film

PD powder was mixed with CV (0.01g/L) solution and stirred for 30 min to ensure complete dissolution. 6.7% aqueous solution of PVA (3 mL), glycerol (1 mL), and DI water (10 mL) added and stirred, then poured into a petri plate and kept in a hot air oven at 60^0 C for 6 h to obtain smooth, transparent and highly flexible film.

III. Characterization

FTIR spectra were recorded on a Shimadzu FTIR spectrophotometer (model 8400 S) as diffused reflectance spectra in KBr dispersion. Wide-angle powder X-ray diffraction (PXRD) data were collected using a Rigaku X-ray diffractometer (model MiniFlex-600) equipped with Cu Kα radiation at 30 kV and 15 mA in the range 2θ=3-80˚ at a rate of 3˚/min. Surface morphology was examined by field emission gun scanning electron microscope (FEGSEM) Make: FEI Ltd., Model: Nova Nano SEM 450 with an accelerating voltage of 20 V to 30 kV.

IV. Cv Release Study

In vitro CV release kinetics was carried out for a period of 24 h. The pre-weighed pieces of PDCV film were placed in 10 mL of release medium, i.e., pH 4, 7, 9, phosphate buffer solution (PBS) and DI water at 25 and 35 °C. After regular time-intervals, film was transferred into fresh release medium, and the amount of CV released was determined spectrophotometrically using a SHIMADZU spectrophotometer model UV-1700 at 560 nm. Drug release kinetics were calculated using the following equations Eq.1-5.

Zero Order:	$Q_t = Q_0 + K_0\, t$	(1)
First-order:	$\ln (1-F) = -K_1\, t$	(2)
Higuchi model:	$F = K_H \times t^{1/2}$	(3)
Hixson-Crowell model:	$\sqrt[3]{(1-F_i)} = 1 - K_\beta\, t$	(4)
Korsmeyer-Peppas model:	$F = K_m\, t^{n}$ or $\ln F = \ln K_m + n \ln t$	(5)

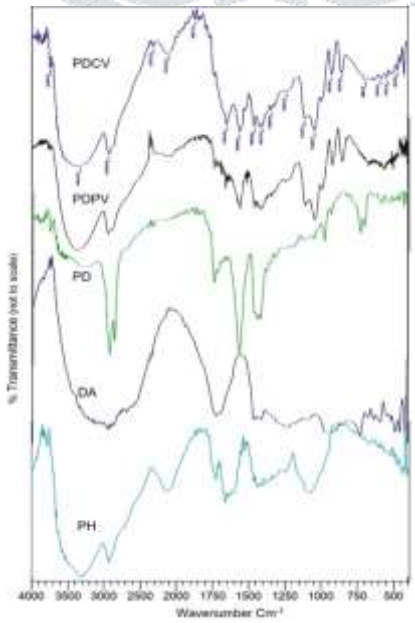
where F=fraction of drug released at time 't', K_0= zero-order release constant, K_1= first-order release constant, K_H =Higuchi constant, F_i=non-released fraction of CV at time Kβ=release constant, Mt=amount of drug released at time 't', M∞ =total amount of CV, K_m =kinetic constant and n=diffusion or release exponent, Q_0 initial amount of drug, Q_t cumulative amount of drug release at time 't'.

V. Results And Discussion

5.1 FTIR spectral analysis

A comparison of the FTIR spectra of PD, DA and PH Fig. 1 revealed a significant reduction in the intensity of broad band (ν_{OH} = 3000-3600 cm^{-1}) corresponding to COOH groups in DA and OH groups of PH in case of PD. Similarly, strong and broad bands due to hydroxyl bending (δ OH around 1600 cm^{-1}) in DA and PH reduced in intensity and shifted to lower wavenumber. A band at 1730 cm^{-1} corresponding to C=O stretch of ester linkage is observed for PD. A comparison of FTIR spectra of PD with PDPV, Fig. 1, indicates the PD was blended with PVA. Characteristic bands of CV ascribed to nC=C and nC-N appeared at 1558 cm^{-1} and 1338 cm^{-1} for PDCV (Cheriaa, Khaireddine, Rouabhia, & Bakhrouf, 2012).

Figure 1. FTIR spectra of PDPV with its constituents and CV loaded film (PDCV)



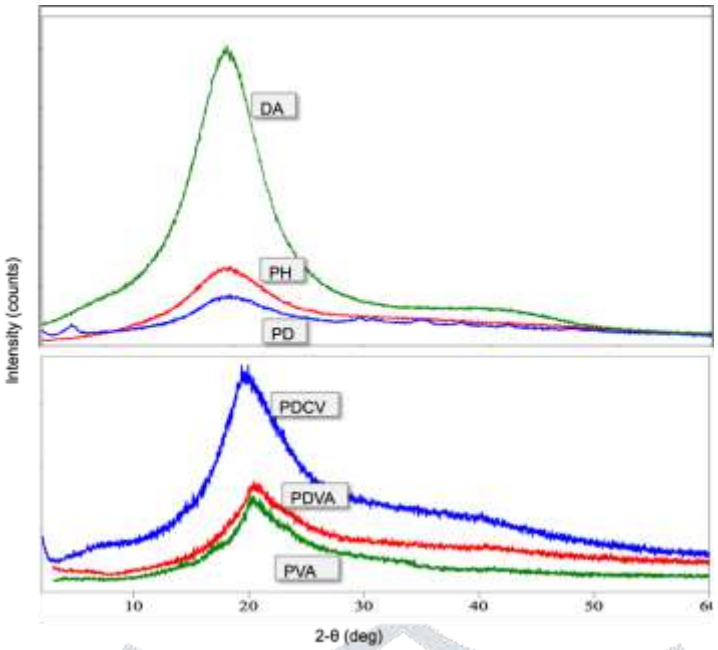
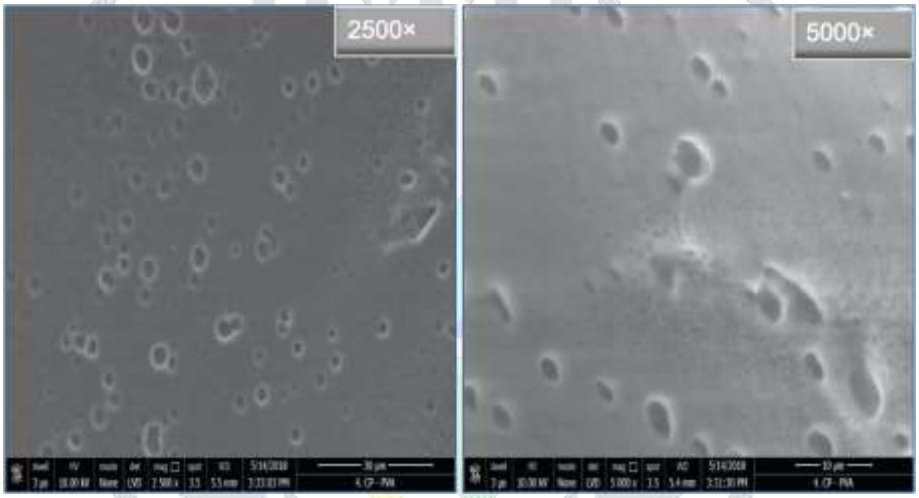


Figure 2 PXRD patterns of PH, DA, PD, PVA, PDPV and PDCV films

Figure 3 SEM images of PDPV at different magnifications



5.2 PXRD and surface morphology studies

PXRD patterns of PDPV and its constituents, PVA, PDPV and PDCV films are presented in Fig. 2. Value of d obtained from PXRD data of PDPV is lowest, which indicated compact assemblage of various ingredients. Next higher value of d is for PDCV due to incorporation of CV in PDPV.

Surface morphology of PDPV was analysed by SEM and the images are shown in Fig. 3. Lighter shade in the SEM images of PDPV shows coverage of surface mainly by hydrophilic domains. Dark elliptical spots are due to hydrophobic DA domains. PDPV is devoid of chemical crosslinker, hence, conformational freedom allows attainment of self-assembly and hydrophilic domains get organized on surface in aqueous medium used for film formation.

5.3 CV release studies

Photographs of CV release are presented in Fig. 4. Plots of % cumulative CV release against time in different media and at 25 and 45 °C in DIW are presented in Fig. 5. It is interesting to note that release of CV was slow and less than 60% was released till 72 h. It was observed as apparent from photograph in Fig. 4 and graphs in Fig. 5 that release was slowest at pH 9.

In order to accept supramolecular carrier systems as drugs, it is essential to predict release kinetics of active substances. Hence, to understand mechanism of drug release, experimental data for *in vitro* CV release was fitted into various theoretical models. Results are presented graphically in Fig. 6 and the calculated parameters are given in Table 1. Correlation coefficients from 0.934 to 0.991 were obtained for the Korsmeyer-Peppas model for CV release. At pH 4, n was calculated to be 0.474 indicating Fickian diffusion, it was 1.563 at pH 9 suggesting a super case-II transport (relaxation/erosion). For all the other cases n was found to be in 0.548 to 0.728 range. Values of n between 0.5 and 1 imply that both the transport mechanisms are involved, i.e., Fickian diffusion and swelling-induced polymer chain relaxation followed by gel surface erosion. This accounts for zero-order release (Manakker et al., 2009). Indeed, r^2 values were found to be greater than 0.9 for curve fitting into zero order model for CV release. Release of CV from PDCV perfectly followed Higuchi drug release model as evident from the r^2 values of nearly 1. Higuchi model is applicable to describe the drug release from several modified pharmaceutical dosage forms, e.g., transdermal systems and water-soluble drug loaded matrix tablets (Higuchi, 1963; Grassi, M., & Grassi, G., 2005).

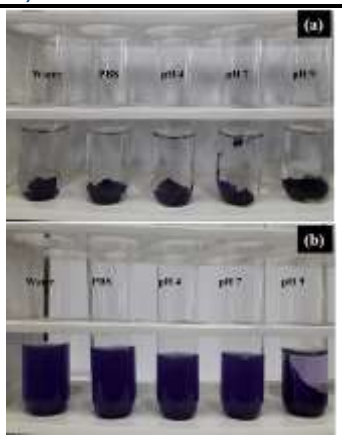


Figure *4 Photographs of CV release in various media (a) initial (b) after 24 h*

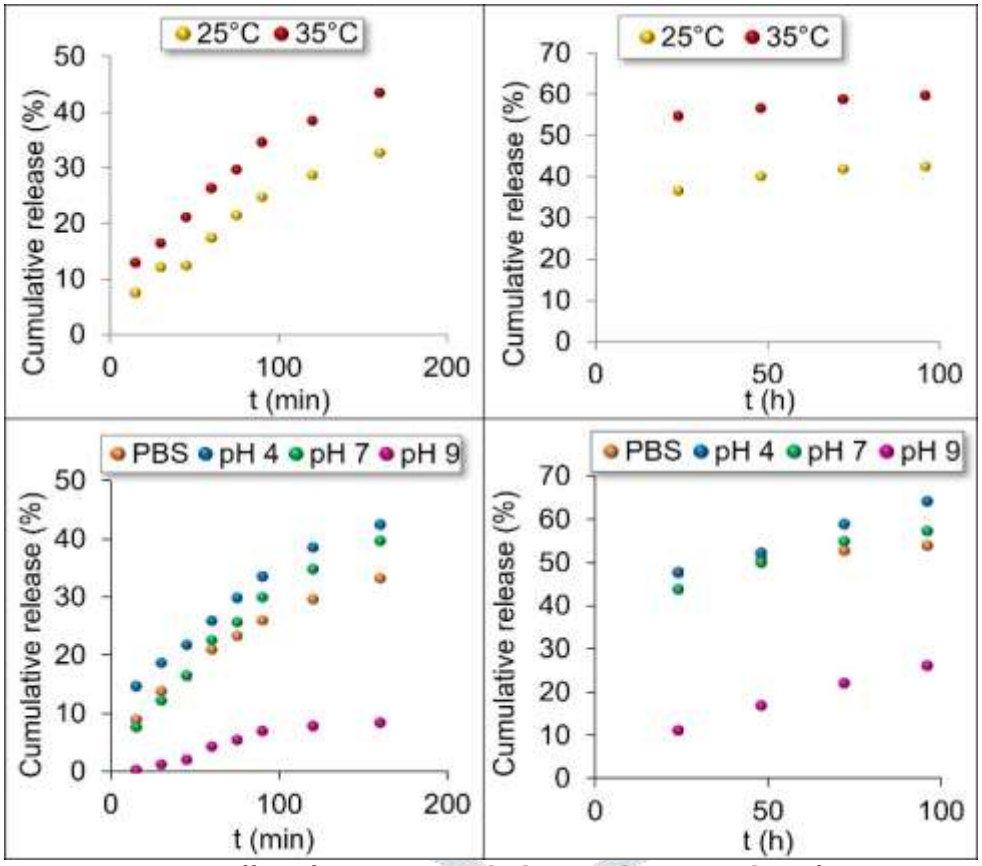


Figure 5 Effect of temperature and release media on CV release from PDCV

Table 1 CV release data in various release media fitted to various theoretical models.

Model	Parameter	PBS	pH 4	pH 7	pH 9	25° C	45° C
Zero order	K	-0.0026	-0.0033	-0.0029	-0.0006	-0.0024	-0.0033
	r^2	0.951	0.942	0.974	0.971	0.971	0.977
First Order	$K_1(min^{-1})$	-0.0021	-0.0021	-0.0030	-0.0083	-0.0243	-0.0068
	r^2	0.967	0.966	0.977	0.950	0.973	0.978
Higuchi	$K_H(min^{-1})$	0.027	0.034	0.030	0.006	0.074	0.034
	r^2	0.999	0.999	0.990	0.929	0.991	0.996
Hixson - Crowell	$K_b(min^{-1})$	-0.0074	-0.0052	-0.0130	-0.0023	-0.0007	-0.0009
	r^2	0.862	0.860	0.668	0.936	0.970	0.972
Korsmeyer - Peppas	n	0.566	0.474	0.728	1.563	0.644	0.548
	r^2	0.994	0.987	0.991	0.934	0.974	0.986

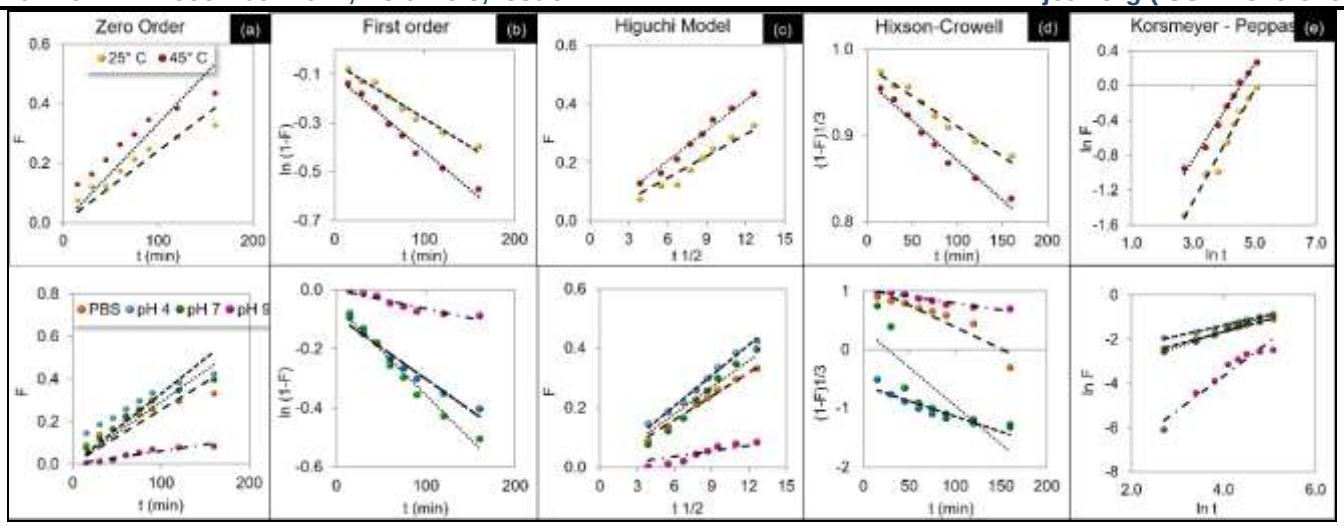


Figure 6 Curve fitting for the theoretical kinetic models applied to the CV release from PDCV film

VI. CONCLUSION

SEM of the film, PDPV indicated self-assembly of hydrophilic and hydrophobic domains. Once the film is formed it does not absorb dyes or metal ions, hence, it effectively restricts entry of chemical contaminants. However, drugs, for example, CV could be easily loaded in PDPV during film formation. Simple preparation, cost effectiveness and slow release of drugs are the attributes of PDPV for application as a good film dressing. Compliance with Higuchi drug release model indicates PDCV to be applicable as transdermal drug release system.

VII. ACKNOWLEDGMENT

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