

PHYSICOCHEMICAL PROPERTIES STUDY OF PLAI PATCHES FOR TOPICAL APPLICATIONS

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ABSTRACT

Objective: The Plai patches were prepared from polymer blends between chitosan/hydroxypropylmethyl cellulose and chitosan/polyvinyl alcohol, and used glycerine as plasticizer. They were possibly evaluated for herbal topical application of *Zingiber cassumunar* Roxb., also called Plai in Thai.

Methods: Plai was extracted with ethanol and evaporated until obtain the dry crude Plai oil. All polymer blends were mixed homogeneously. The crude Plai was dissolved in absolute ethanol and mixed together in polymer blends solutions by traditional beaker method until homogeneous in appearance. They were transferred into Petri-dish and dried in hot air oven at 70±2°C for 5 hours. They were tested the moisture uptake and swelling values, ATR-FTIR, SEM, DSC, and XRD.

Results: The moisture uptake and swelling ratio values were 0.2851 – 0.2918 and 0.2093 – 0.2391, respectively. The Plai patches showed the suitable physicochemical properties with comprised of various functional groups of polymer blends from ATR-FTIR, showed the single peak from DSC, and showed the amorphous phase from XRD. In addition, they were ruggedness on the surface and high dense in cross section of the Plai patches.

Conclusion: We successfully prepared the Plai patches from different polymer blends which were chitosan/hydroxypropylmethyl cellulose blends and chitosan/polyvinyl alcohol blends by traditional beaker preparation. The physicochemical properties of the Plai patches were suitable to use for topical application.

Keyword: Chitosan, Hydroxypropylmethyl Cellulose, Polyvinyl Alcohol, Polymer Blends, Physicochemical Properties.

INTRODUCTION

Polymer patches are now effective alternative products for topical systems to deliver active compound to skin. For the development of topical systems, polymer selection and product design are important since they directly affect the physicochemical properties, compatibility, and stability of the obtained products [1]. Various research reports the many types of polymers such as cellulose derivatives [2], polyvinyl alcohol [3], chitosan [4], polyacrylate [5], deproteinized natural rubber latex [6-14] are being used as materials to apply to the skin as gelling agents, thickening agents, and film formers to control drug release [1].

The Thai Herbal Compress ball, also known as Herbal Ball or Luk Pra Kob, has been used for more than 400 years in Thailand and in Thai traditional fields. It is a ball of Thai herbs used as a hot compress to relieve aches, inflammation, and pains of the body by opening the pores and bringing a medicinal heat to muscles to induce relaxation.

It is composed of various dried herbs such as *Zingiber cassumunar* Roxb., *Curcuma longa* Linn., *Citrus hystrix* DC., *Cymbopogon citratus* Stapf., *Acacia rugata* Merr., and *Tamarindus indica* Linn. These are wrapped in cotton traditionally used in Thai medicine [15-17].

Zingiber cassumunar Roxb., as known as Plai in Thai, is the main herb in Thai Herbal Compress ball used for the treatment of asthma, as well as for muscle and joint pain. The volatile oil of (*E*)-4-(3', 4'-dimethoxyphenyl)-but-3-en-1-ol was extracted from the rhizomes of Plai. It was found to exhibit inhibitory and anti-inflammation activity by using various experimental models of inflammation [18, 19]. Analgesic and antipyretic properties of (*E*)-4-(3', 4'-dimethoxyphenyl)-but-3-en-1-ol were also reported [19-21]. It is also used as topical treatment for sprains, contusions, joint inflammations, muscular pain, abscesses, and similar inflammation-related disorders [22, 23].

The main objective of this work was to prepare the Plai patches that made from polymer blends between chitosan/hydroxypropylmethyl cellulose and chitosan/polyvinyl alcohol, and used glycerine as plasticizer. They were tested the physicochemical properties such as moisture uptake and swelling ratio values, scanning electron microscopy (SEM), attenuated total reflection fourier transform infrared spectroscopy (ATR-FTIR), differential scanning calorimeter (DSC), and X-ray diffractometry (XRD) studies possibly evaluated for herbal topical application.

MATERIALS AND METHODS

Materials

Plai was purchased from Charoensuk Osod, Thailand. Chitosan was purchased from Seafresh Industry Public Co., Ltd, Thailand. Hydroxypropylmethyl cellulose was purchased from Onimax, Thailand. Polyvinyl alcohol (*M_w* = 195,000 g/mol) and glycerine were purchased from Sigma-Aldrich, USA. All organic solvents were of analytical grade obtained from Merck KGaA, Germany.

Plai patches preparation

The chitosan was dissolved in concentration of 3.5%w/v in distilled water comprised of 1% acetic acid. The hydroxypropylmethyl cellulose or polyvinyl alcohol was dissolved in distilled water in concentration of 20%w/v. Then, 2 g of 3.5%w/v chitosan was mixed together with 5 g of 20%w/v of hydroxypropylmethyl cellulose or polyvinyl alcohol, and mixed homogeneously mixed with glycerine as plasticizer.

After that, the crude Plai was dissolved in absolute ethanol and continuously mixed in polymer blends solution. They were transferred into Petri-dish and dried in hot air oven at 70±2°C for 5 hours. They were tested the moisture uptake and swelling values, SEM, ATR-FTIR, DSC, and XRD.

Moisture uptake and swelling ratio studies

For moisture uptake, the Plai patches were cut into 1 cm × 1 cm of specimens. These specimens were weighed (W_0) and moved to stability chamber (model: Climate Chamber ICH/ICH L, Memmert GmbH + Co. KG, Germany) which controlled the temperature at 25°C and 75% relative humidity environment. They were taken out and weighed every week until their weight was constant (W_u). The percentage of moisture uptake was calculated by equation [24].

$$\text{Moisture uptake} = \frac{(W_u - W_0)}{W_0}$$

For the swelling ratio, the 1 cm × 1 cm specimens were weighed (W_0) and immersed in 5 mL of distilled water and moved to stability chamber (model: Climate Chamber ICH/ICH L, Memmert GmbH + Co. KG, Germany) which controlled the temperature at 25°C and 75% relative humidity environment. After removal of excess water, the hydrated films were reweighed (W_s), then dried at 60 ± 2°C overnight, and weighed again (W_d). The swelling ratio was calculated by equation.

$$\text{Swelling ratio} = \frac{(W_s - W_0)}{W_0}$$

SEM photography

The Plai patches surface and cross section were photographed by SEM (model: Quanta 400, FEI, Czech Republic) with high vacuum and high voltage of 20 kV condition, and using everhart thornley detector (ETD).

ATR-FTIR study

The chitosan film, hydroxypropylmethyl cellulose film, polyvinyl alcohol film, crude Plai, and Plai patches were examined using the ATR-FTIR technique. They were scanned at a resolution of 4 cm⁻¹ with 16 scans over a wavenumber region of 400 - 4000 cm⁻¹ using the FT-IR spectrometer (model: Nicolet 6700, DLATGS detector, Thermo Scientific, USA.). The characteristic peaks of IR transmission spectra were recorded.

DSC study

A DSC was used to investigate the endothermic transition of the substances that also confirmed the compatibility of each ingredient. A 5 - 10 mg of film was transferred into the DSC pan that was then hermetically sealed, and run in the DSC instrument (model: DSC7, Perkin Elmer, USA) from 20°C to 350°C at the heating rate of 10°C/min under a liquid nitrogen atmosphere. The DSC thermogram was reported, and the endothermic transition was investigated.

XRD study

The XRD (model: X'Pert MPD, PHILIPS, Netherlands) was also employed to study the compatibility of the chitosan, hydroxypropylmethyl cellulose, polyvinyl alcohol, and Plai patches. The generator operating voltage and current of X-ray source were 40 kV and 45mA, respectively, with an angular of 5 - 40° (2θ), and a stepped angle of 0.02° (2θ)/s.

RESULTS AND DISCUSSION

The moisture uptake and swelling ratio values of chitosan film was 0.2340±0.0493 and 0.1970±0.0704, respectively. When chitosan was blended with hydroxypropylmethyl cellulose or polyvinyl alcohol, they were significantly increased the moisture uptake and swelling ratio values to 0.2918±0.0206 and 0.2391±0.0442, respectively for chitosan/hydroxypropylmethyl cellulose/glycerine/crude Plai blends, and 0.2851±0.0078 and 0.2093±0.0588, respectively for chitosan/polyvinyl alcohol/glycerine/crude Plai blends. The moisture uptake and swelling ratio play important roles during the early stages of patches degradation [25]. These results were related with other publication that reported the hydroxypropylmethyl cellulose or polyvinyl alcohol blended to another polymer blends [6-10, 12]. They can increase the hydrophilicity of polymer blends in term of moisture uptake, as well as they can increase the swelling ratio because some hydrophilic parts could be dissolved and eroded from the patches, to increase the number of porous channels. An ATR-FTIR spectrum, in Fig. 1 shows the completely major functional groups of chitosan, hydroxypropylmethyl cellulose or polyvinyl alcohol, and crude Plai in Plai patches. Thus, it could be confirmed the successful identify of Plai patched indicated the no changeable of each ingredient in the Plai patches [26].

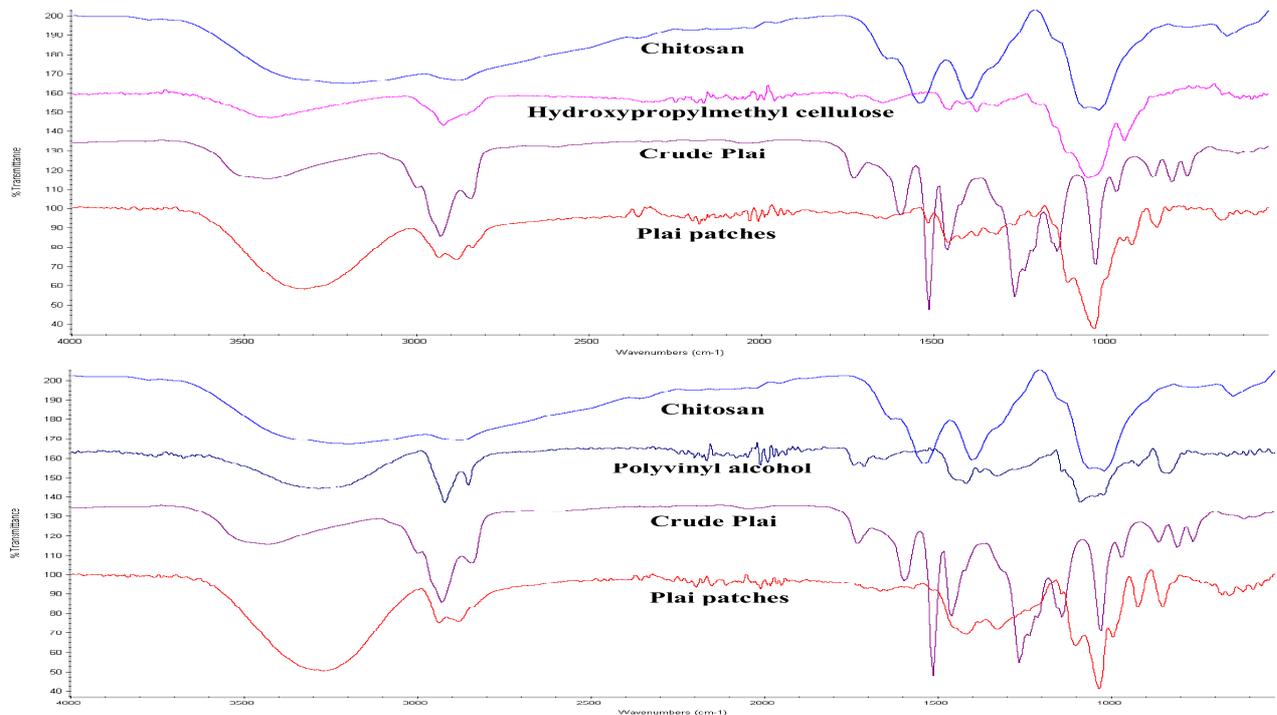


Fig. 1: The ATR-FTIR spectra of various polymer blends with composed of chitosan/hydroxypropylmethyl cellulose (top) and chitosan/polyvinyl alcohol (below)

Table 1: The temperature transition detected by DSC

	Peak I (°C)			Peak II (°C)		
	Onset	Peak	End	Onset	Peak	End
Chitosan	25.666	70.333	107.965	306.405	323.666	333.666
Chitosan/hydroxypropylmethyl cellulose/glycerine/crude Plai	62.462	138.880	168.015	200.859	271.833	292.546
Chitosan/polyvinyl alcohol/glycerine/crude Plai	43.359	92.333	149.638	213.856	261.000	283.359

The behavior of chitosan, chitosan/hydroxyl propylmethyl cellulose/glycerine/crude Plai, and chitosan/polyvinyl alcohol/glycerine/crude Plai were observed in the DSC thermograms (Fig. 2 and Table 1) which also indicated that all the ingredients in the Plai patches were compatible [27].

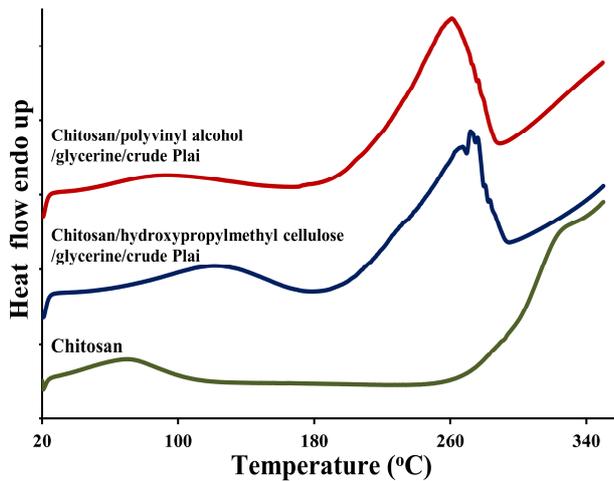


Fig. 2: The DSC thermograms of various polymer blends with composed of chitosan/hydroxypropylmethyl cellulose and chitosan/polyvinyl alcohol

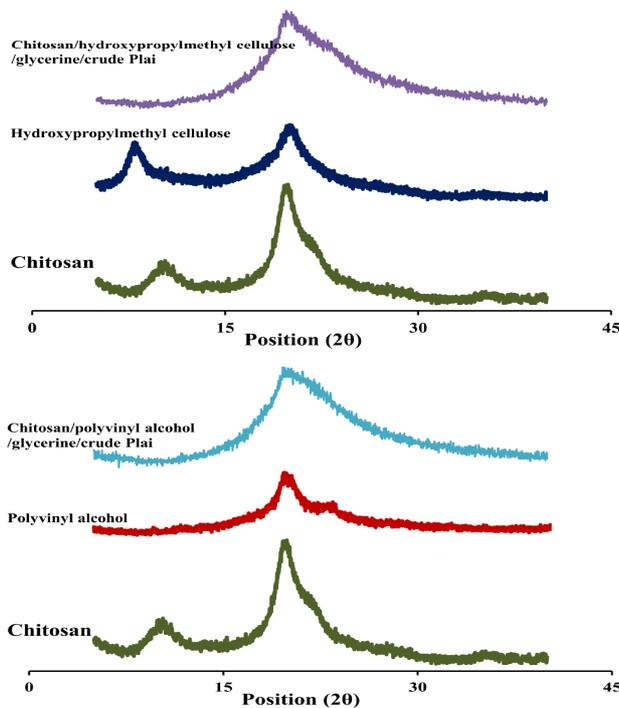


Fig. 3: The XRD patterns of various polymer blends with composed of chitosan/hydroxypropylmethyl cellulose (top) and chitosan/polyvinyl alcohol (below)

The XRD patterns of the chitosan, hydroxyl propylmethyl cellulose, polyvinyl alcohol, chitosan/hydroxyl propylmethyl cellulose/glycerine/crude Plai, and chitosan/polyvinyl alcohol/glycerine/crude Plai were studied between 5 - 40° (2θ) are shown in Fig. 3. We found the intensity results of pure chitosan at 10.33° and 19.59°, hydroxyl propylmethyl cellulose at 7.95° and 20.13°, and polyvinyl alcohol at 19.69° represented their semicrystalline characters because of the strong intermolecular interaction between hydroxyl propylmethyl cellulose or polyvinyl alcohol chains through intermolecular hydrogen bonding [28]. In addition, these peaks were not found in the Plai patches which exhibited an amorphous phase. These indicated the miscibility of polymer blends between various ingredients in their patches.

The SEM was used to confirm the high resolution morphology in each Plai patches (Fig. 4). The Plai patches produced ruggedness on the surface and high density without poring, cracking, or cavities in cross section.

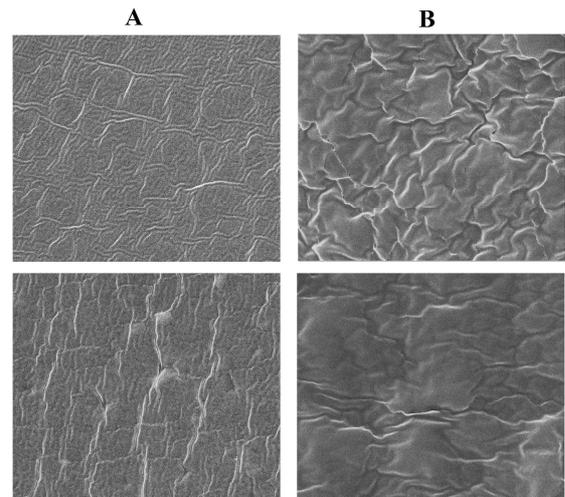


Fig. 4: The surface (1,500x) (A) and cross section (5,000x) (B) of Plai patches with composed of chitosan/hydroxypropylmethyl cellulose (top) and chitosan/polyvinyl alcohol (below)

CONCLUSION

We successfully prepared the Plai patches from different polymer blends which were chitosan/hydroxypropylmethyl cellulose blends and chitosan/polyvinyl alcohol blends, and glycerine was used as plasticizer by traditional beaker method. The Plai patches showed the best potential for novel materials. The physicochemical properties such as moisture uptake and swelling ratio values, ATR-FTIR, DSC, and XRD studies indicated the compatibility of the blended ingredients. Thus, these results have provided clear evidence for the feasibility of the Plai patches could be used suitably for topical application and the *in vitro* studies may evaluate in the further.

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REFERENCES

- Barry BW. Novel mechanisms and devices to enable successful transdermal drug delivery. *Eur J Pharm Sci* 2001; 14(2): 101-14.
- Ito T, Yeo Y, Highley CB, Bellas E, Benitez CA, Kohane DS. The prevention of peritoneal adhesions by *in situ* cross-linking hydrogels of hyaluronic acid and cellulose derivatives. *Biomaterials* 2007; 28(6): 975-83.
- Seabra AB, de Oliveira MG. Poly(vinyl alcohol) and poly(vinyl pyrrolidone) blended films for local nitric oxide release. *Biomaterials* 2004; 25(17): 3773-82.
- He W, Guo X, Xiao L, Feng M. Study on the mechanisms of chitosan and its derivatives used as transdermal penetration enhancers. *Int J Pharm* 2009; 382(1-2): 234-43.
- Minghetti P, Cilirzo F, Montanari L. Evaluation of adhesive properties of patches based on acrylic matrices. *Drug Dev Ind Pharm* 1999; 25(1): 1-6.
- Pichayakorn W, Suksaeree J, Boonme P, Amnuait T, Taweepreda W, Ritthidej GC. Deproteinized natural rubber as membrane controlling layer in reservoir type nicotine transdermal patches. *Chem Eng Res Des* 2012; 91(3): 520-29.
- Pichayakorn W, Suksaeree J, Boonme P, Amnuait T, Taweepreda W, Ritthidej GC. Reservoir type nicotine transdermal patches using deproteinized natural rubber as membrane controlling systems: Effect of polymer and plasticizer blends. *In manuscript submission* 2012.
- Pichayakorn W, Suksaeree J, Boonme P, Taweepreda W, Ritthidej GC. Preparation of deproteinized natural rubber latex and properties of films formed by itself and several adhesive polymer blends. *Ind Eng Chem Res* 2012; 51(41): 13393-404.
- Pichayakorn W, Waiprib R, Lueanpaen I, Suksaeree J, Taweepreda W. Physicochemical properties of pseudolatex systems prepared from para rubber sheet and preliminary drug loading for drug delivery. *Thai J Pharm Sci* 2013; 38: 260-64.
- Suksaeree J, Boonme P, Taweepreda W, Ritthidej GC, Pichayakorn W. Characterization, *in vitro* release and permeation studies of nicotine transdermal patches prepared from deproteinized natural rubber latex blends. *Chem Eng Res Des* 2012; 90(7): 906-14.
- Suksaeree J, Charoenchai L, Monton C, Chusut T, Sakunpak A, Pichayakorn W, et al. Preparation of a pseudolatex-membrane for ketoprofen transdermal drug delivery systems. *Ind Eng Chem Res* 2013; 52(45): 15847-54.
- Suksaeree J, Monton C, Sakunpak A, Charoonratana T. Formulation and *in vitro* study of ketoprofen pseudolatex gel for transdermal drug delivery systems. *Int J Pharm Pharm Sci* 2014; 6(2): 248-53.
- Suksaeree J, Pichayakorn W, Monton C, Sakunpak A, Chusut T, Saingam W. Rubber polymers for transdermal drug delivery systems. *Ind Eng Chem Res* 2014; 53(2): 507-13.
- Suksaeree J, Pichayakorn W, Monton C, Sakunpak A, Chusut T, Saingam W, et al. Formulation of ketoprofen matrix membrane for transdermal delivery systems. *Thai J Pharm Sci* 2013; 38: 180-83.
- Panomhom R, Thiengkamol N, Thiengkamol T, Kurukod J. A study of knowledge, practice and satisfaction of herbal compressed ball use through workshop for health volunteer. *Eur J Soc Sci* 2012; 31(4): 550-57.
- Suksaeree J, Charoenchai L, Kraisintu K, Songsak T, Pichayakorn W, Boonme P. The extraction method and formulation of *Zingiber cassumunar* Roxb. (Plai): A review. *Bull Health Sci Tech* 2013; 11(1): 19-22.
- Suksaeree J, Charoenchai L, Pichayakorn W, Boonme P. HPLC method development and validation of (*E*)-4-(3,4-dimethoxyphenyl)-but-3-en-1-ol in *Zingiber cassumunar* Roxb. from Thai Herbal Compress ball. *Int J Pharm Pharm Sci Res* 2013; 3(3): 115-17.
- Kanjanapothi D, Soparat P, Panthong A, Tuntiwachwuttikul P, Reutrakul V. A uterine relaxant compound from *Zingiber cassumunar*. *Planta Med* 1987; 53: 329 - 32.
- Panthong A, Kanjanapothi D, Niwatananant W, Tuntiwachwuttikul P, Reutrakul V. Anti-inflammatory activity of compound D {(*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-2-ol} isolated from *Zingiber cassumunar* Roxb. *Phytomedicine* 1997; 4(3): 207-12.
- Ozaki Y, Kawahara N, Harada M. Anti-inflammatory effect of *Zingiber cassumunar* Roxb. and its active principles. *Chem Pharm Bull (Tokyo)* 1991; 39(9): 2353-59.
- Panthong A, Kanjanapothi D, Niwatananun V, Tuntiwachwuttikul P, Reutrakul V. Anti-inflammatory activity of compounds isolated from *Zingiber cassumunar*. *Planta Med* 1990; 56(6): 655.
- Pongprayoon U, Soontornsaratune P, Jarikasem S, Sematong T, Wasuwat S, Claeson P. Topical antiinflammatory activity of the major lipophilic constituents of the rhizome of *Zingiber cassumunar*. Part I: The essential oil. *Phytomedicine* 1997; 3(4): 319-22.
- Pongprayoon U, Tuchinda P, Claeson P, Sematong T, Reutrakul V, Soontornsaratune P. Topical antiinflammatory activity of the major lipophilic constituents of the rhizome of *Zingiber cassumunar*. Part II: Hexane extractives. *Phytomedicine* 1997; 3(4): 323-26.
- Rajesh N, Siddaramaiah H, Gowda DV, Somashekar CN. Formulation and evaluation of biopolymer based transdermal drug delivery. *Int J Pharm Pharm Sci* 2010; 2(Suppl. 2): 142-47.
- Limpongsa E, Umprayn K. Preparation and evaluation of diltiazem hydrochloride diffusion-controlled transdermal delivery system. *AAPS PharmSciTech* 2008; 9(2): 464-70.
- Bianchi SE, Angeli VW, Souza KCBd, Miron DdS, Carvalho GdA, Santos Vd, et al. Evaluation of the solubility of the HPMC: PVA blends in biological fluids *in vitro*. *Mat Res* 2011; 14: 166-71.
- Naskar AK, De PP, *Applications of DSC and TGA for the characterisation of rubbers and rubbery materials*, in *Thermal Analysis of Rubbers and Rubbery Materials*, Choudhury NR, De PP, Dutta NK, Editors. 2010, Smithers Rapra Technology: Shropshire. p. 65-148.
- Abdelaziz M, Ghannam MM. Influence of titanium chloride addition on the optical and dielectric properties of PVA films. *Phys B* 2010; 405(3): 958-64.