Project 1

Vildagliptin plasticized hydrogel film in the control of ocular inflammation after topical application: study of hydration and erosion behaviour

Vildagliptin (VID) is a dipeptidyl peptidase-4 (DPP-4) inhibitor used in controlling blood glucose level in type 2 diabetes. Vildagliptin improves beta cells function and is also suggested to effectively control the inflammation. The possible ocular anti-inflammatory property of vildagliptin has been explored using topically applied plasticized ocular film formulation. Film formulation was prepared by solvent cast and evaporation method using triethanolamine (TEA), dimethyl sulphoxide (DMSO), and polyethylene glycol 400 (PEG 400) as the plasticizer in HPMC hydrogel matrix base. Anti-inflammatory study was carried out in the carrageenan induced ocular rabbit model. Analytical methods confirmed that the drug was present almost in completely amorphized form in the film formulation. Level of hydration, swelling and erosion rate of the film played the controlling factor in the process of drug release, ocular residence and permeation. Maximum swelling rate of 363 h−1 has been shown by VHT compared to other formulation of VHD and VHP (174 and 242 h−1 respectively). Film containing DMSO exhibited highest in vitro release as well as ex vivo ocular permeation. Film formulation has shown a fast recovery of ocular inflammation in contrast to the untreated eye after inducing inflammation. Plasticized vildagliptin hydrogel film formulation could be utilized in the management and control of ocular inflammation particularly with diabetic retinopathy after proper clinical studies in higher animal and human individuals.

Project 2

Influence of TiO2 on Mucosal Permeation of Aceclofenac: Analysis of Crystal Strain and Dislocation Density

Titanium dioxide can adhere with human epithelial cells and have good tolerability. Present work has been undertaken to explore the influence of TiO2 on mucosal permeation of aceclofenac. Mucosal permeation of aeclofenac solution containing TiO2 has been carried out. In fourier transform infrared spectrosopy (FTIR), the intensity of the peaks has decreased along with the increase of TiO2 content in the formulation indicating a possible binding between drug and TiO2. Melting enthalpy has been decreased with the increased content of TiO2 in the solid. The status of crystal strain and dislocation density of TiO2 and aceclofenac in the solid state formulation has also been evaluated from Xray Diffraction data using Debye-Scherrer's equation. Mucosal permeation of aceclofenac has shown sustained effect for more than 20 h in presence of titanium dioxide. Titanium dioxide could be used in designing formulation for sustaining mucosal aceclofenac delivery after performing risk assessment study.

Project 3

Quantitative Estimation of Tabletability of Aceclofenac after Incorporation of Titanium Dioxide using Area under the Curve

Tablet manufacturing with direct compression is one of the leading industrial technique that consumes less time, labour and economic also. But the choice of excipients are critical in this case which will allow the drug to get compressed without granulation techniques. **Purpose:** Aceclofenac is a BCS class II non-steroidal anti-inflammatory drug, which exerts a low oral bioavailability because of low solubility in aqueous medium. The drug also suffers from compressibility and also shows poor tabletibility. **Methods:** We have attempted to improve tabletability by incorporating titanium dioxide (TiO2) through kneading and solvent evaporation technique. **Results:** In the FTIR study revealed that NH and Cl aromatic stretching of aceclofenac has been affected significantly due to binding with TiO2. DSC thermogram ascertained the partial amorphization of the drug in the formulations. Evaluated tabletability from the area under the applied pressure vs tensile strength curve (AUTC) of A1T1 has shown a poor value in contrast to other formulations.

Project 4

Interactions between Ibuprofen and Silicified-MCC: Characterization, Drug Release and Modeling Approaches

Analysis of the binding interactions of ibuprofen and silicified-microcrystalline cellulose (SMCC) has been undertaken. Co-processing of ibuprofen with SMCC was carried out by solid state ball milling, and aqueous state equilibration followed by freeze drying to investigate the effect of silicified-microcrystalline cellulose on ligand. Molecular docking study revealed that ibuprofen formed complex through hydrogen bond with microcrystalline cellulose (MCC) and silicon dioxide (SiO2); the binding energy between MCC and SiO2, and ibuprofen and SMCC were found as –1.11 and –1.73 kcal/mol respectively. The hydrogen bond lengths were varying from 2.028 to 2.056 A. Interaction of Si atom of SMCC molecule with Pi-Orbital of ibuprofen has shown the bond length of 4.263 A. Significant improvement in dissolution of ibuprofen has been observed as a result of interaction. Binary and ternary interactions revealed more stabilizing interactions with ibuprofen and SMCC compared to SMCC formation.

Project 5

Sustained Release Bioadhesive Suppository Formulation for Systemic Delivery of Ornidazole: In-silico Docking Study

Background and Objectives: Ornidazole is widely used as an antiprotozoal and antiamoebic drug and its onset of action is within 2 h. The major extent of the drug is metabolized in the liver and excreted in the urine and faeces. Hence, the present study of suppository formulation for sustained systemic delivery of ornidazole is significant which could minimize abdominal disturbances and nausea and delayed onset of action particularly after oral administration. **Methods:** Bioadhesive suppository formulations were prepared for systemic delivery of ornidazole via rectal and vaginal route. **Results:** The physical drug-excipient-interaction was confirmed by in-silico docking study. The affinity between drug-HPMC and drug-PEG was found to be -2 and -0.9 k cal/mol respectively. In vitro drug release of the

suppositories varied depending on the viscosity grade of HPMC used and all have followed mostly diffusion controlled mechanism. The formulation containing HPMC K100 showed the most sustained release of ornidazole in both the dissolution fluid of pH 7.4 and 4.5 (54.53 and 41.89 % respectively after 360 min). **Conclusion:** In conclusion, present bio adhesive suppositories could be utilized for sustained systemic delivery of ornidazole via rectal and vaginal route. The findings of this work will contribute to the current knowledge and encourage future pre-clinical research.

Project 6

Budesonide-Cyclodextrin in Hydrogel System: Impact of Quaternary Surfactant on *in vitro-in vivo* Assessment of Mucosal Drug Delivery

Budesonide, a glucocorticosteroid is generally used to treat chronic inflammation and asthma. Hepatic first-pass metabolism and poor solubility are the major causes of its limited oral bioavailability. Present work was undertaken for the preparation of hydrogel film formulation with cyclodextrin complexation of budesonide containing quaternary surfactant for possible enhancement of mucosal permeation. FTIR study confirmed drug-polymer hydrogen bonding. Almost complete amorphization of the drug was pronounced by SEM, DSC and XRD studies. The film containing benzalkonium and hydroxypropyl beta-cyclodextrin exhibited in vitro dissolution and mucosal permeation to the highest extent of 87.2 and 95.8 % respectively in contrast to the others. Film formed hydrogel in aqueous mucin and enhanced the mucosal tissue residence time due to the mucoadhesive nature of the polymer. Acute inflammation in the rabbit eye was controlled within 3 h by applying the film in the cul-de-sac. The presence of cyclodextrin and quaternary surfactant brought about significantly improved drug release and mucosal permeation compared to their absence in the HPMC film. Hydrogel formed in aqueous mucin enhanced the mucosal residence time and controlled acute inflammation in the rabbit eye within 3 h after topical application.

Project 7

Characterization of Hydration Behaviour and Modeling of Film Formulation

Hydration behavior of hydrogel-based polymeric film possesses great importance in mucosal drug delivery. Modified Lag phase sigmoid model was used for the investigation of hydration of the film. Kaolin incorporated HPMC K100LVCR (HL) and K100M (HH) films containing dexamethasone as a model drug have been prepared for studying swelling kinetics. Swelling of HL and HH films was decreased with the gradual increase of kaolin content and HH of higher viscosity has shown higher value than HL matrix. Kaolin also inhibited the film erosion process. Mathematically modified lag phase sigmoid model demonstrated similarity of the predicted swelling content with the observed value. High R2 and small RMSE value confirmed the successful fitting of the modified lag phase sigmoid model to the experimental data of swelling content. τ value similar to the observed one was obtained. This modified model could be reliable enough for estimating hydration process in food grains, food packaging films etc.

Project 8

3D printing in managing supply disruptions related to COVID-19 pandemic: Food and Drug Administration's current thinking on regulation

Recent developments and collaborations of pharmaceutical manufacturers, hospitals, and government funded research bodies using 3D printing technology have been highlighted for the management of the healthcare crisis. 3D printing is a process of converting virtual 3D models developed by computer aided design into physical forms upon addition of material layer-by-layer (also known as additive manufacturing). This 3D printing is supposed to revolutionize significantly the healthcare system in the coming years. This process involves a tailored deposition of biomaterials layer by layer such as polylactic acid (PLA), polyvinyl alcohol (PVA), or other suitable pharma-grade polymers, copolymers, and their combinations to formulate three-dimensional custom designs with controlled architecture and composition. Food and Drug Administration (FDA) is currently thinking on regulation to ease the import restrictions for products intended for the detection and diagnosis of COVID-19 to ensure the timely availability of test kits.

Project 9

Bentonite clay incorporated topical film formulation for delivery of trimetazidine: Control of ocular pressure and in vitroin vivo correlation

Bentonite clay based film formulation has been prepared for topical delivery of trimetazidine (TZ) for the control of ocular pressure. Trimetazidine ophthalmic film formulation has been prepared incorporating bentonite at 1: 0.0001 to 1: 0.00005 ratio in hydroxylpropyl methylcellulose (HPMC) matrix by solvent casting method. Film formulation showed controlled release of drug and thereby extending the ophthalmic permeation for more than 6 h. Permeation has been extended with the decrease of bentonite amount in the film. Sustained trimetazidine delivery has been characterized by the area under the decreased intraocular pressure (IOP) versus time curve after topical administered film formulation. In rabbits treated with film formulation TB3, the peak IOP dropped of almost 30 % from the baseline at 240 min and persisted until 360 min and a good in vitro-in vivo correlation has also been established. The matrix formulation containing bentonite has shown higher negative biding energy values compared to the formulation without containing bentonite indicating stable interaction with improved bioavailability and sustained effect. Bentonite incorporated trimetazidine film formulation could be utilized in the control and management of intraocular pressure in rabbit.

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