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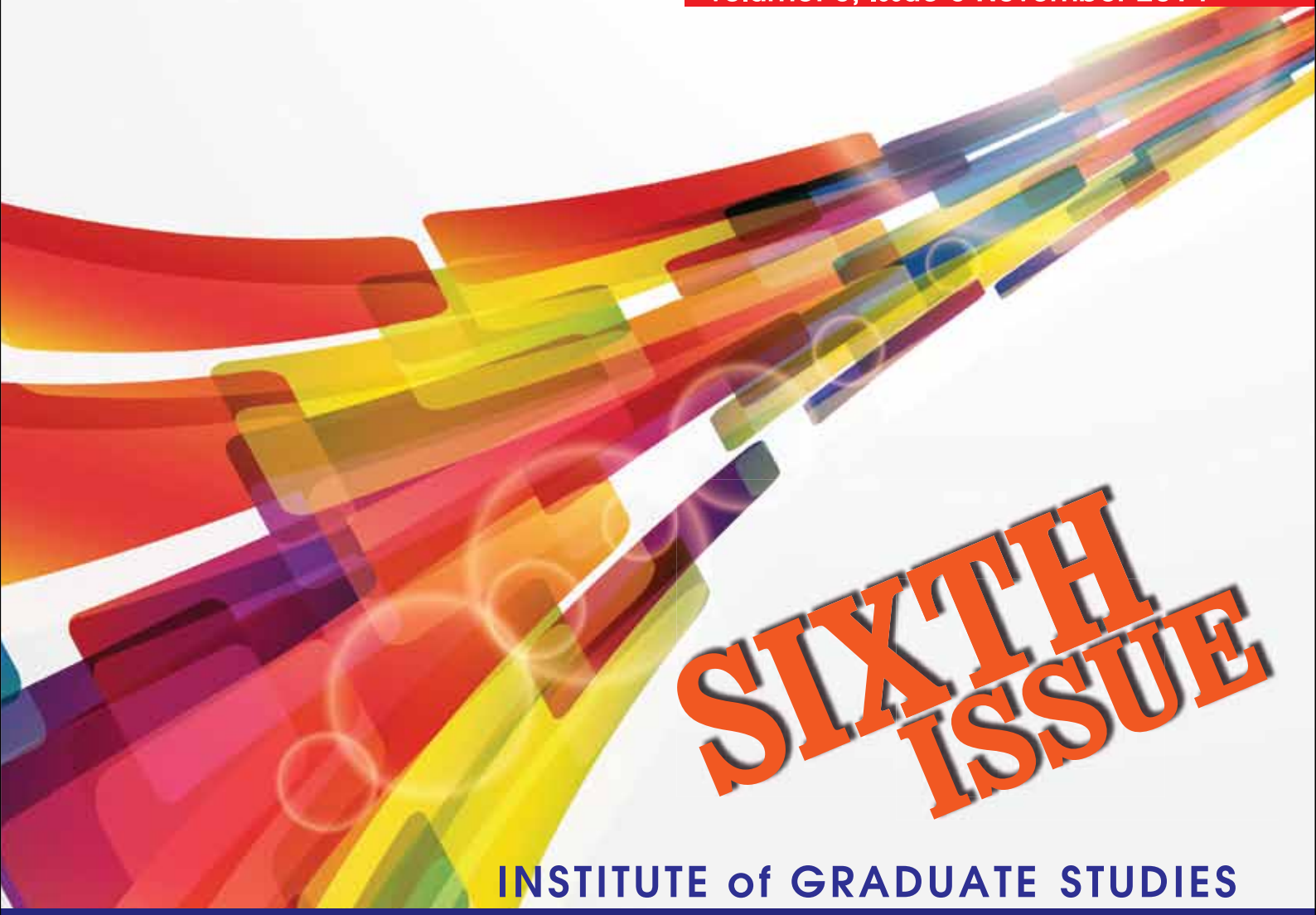

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Name :
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Title :
Colon-Specific Delivery Of 5-Fluorouracil From Zinc Pectinate Spheroids Through *In Situ* Intra-Capsular Ethylcellulose-Pectin Plug Formation

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Conventional fluid-bed and immersion film coating of hydrophilic zinc pectinate spheroids using ethylcellulose-pectin mixture is met with fast drug release due to hydrophobic ethylcellulose coat detachment. This study explored *in situ* intra-capsular spheroid coating for colon-specific delivery of 5-fluorouracil. The solid coating powder was constituted of ethylcellulose and pectin in weight ratios of 11:0 to 2:9. Its weight ratio to spheroids was varied between 2:3 and 3:2. Delayed 5-fluorouracil release was obtained when the weight ratio of ethylcellulose and pectin in coating powder was kept at 8:3, and weight ratio of solid coating powder to spheroids was kept at 3:2 with particle size of ethylcellulose reduced to 22 μm. *In situ* intra-capsular wetting of pectin coat by dissolution medium resulted in the formation of ethylcellulose plug interconnecting with spheroids through the binding action of pectin. The majority of drug was released in the colon

region and complete drug release was obtained through digestion of core spheroids by pectinase. Through *in vivo* pharmacokinetic and pharmacodynamic studies, the intra-capsular coated spheroids were found to be able to reduce the drug bioavailability, enhance its accumulation at colon and reduce both number and size of tumor through reforming the tubular epithelium with basement membrane and restricting the expression of cancer from adenoma to adenocarcinoma. Given a dosage regimen of 15 mg/kg/day for 5 days in rats, the intra-capsular coated spheroids also eliminated the formation of aberrant crypt foci which represented a putative preneoplastic lesion in colon cancer, unlike other treatment modes. Inferring from blood levels of hemoglobin, red blood cell, white blood cell, hematocrit, mean corpuscular hemoglobin, platelet, urea, creatinine, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase and bilirubin, intra-capsular spheroid coating to target 5-fluorouracil delivery at cancerous colon is concluded as a feasible colon cancer formulation approach with reduced risks of systemic adversity.