Isabgol of the formulation. interpenetrating polymer network (ipn)

Isabgol and PolyVinyl Alcohol (PVA) Interpenetrating Polymer Network (IPN) for the ControlledRelease of Diclofenac sodium 1)Introduction- Polymer which arebiodegradable and biocompatible are widely used for the sustained or controlleddrug delivery of the drug. when we used natural and synthetic polymer alonethen that are not able to fulfill the all demands of the particular deliverysystem.

Now a day the natural polymers are widely used in the pharmaceuticalmarket just because of their lower cost, lesser toxicity, biodegradable andbiocompatible property. The safety margin of the natural polymer is also high. But in comparison with synthetic polymers the physicochemical property ofnatural polymer is poor. so, by combining the physical and chemical propertiesof two different polymer may provide a significant advantage in the drugdelivery system that can be achieved by combining the synthetic and naturalpolymer. Such type of combination is very helpful in sustaining the release ofthe drug which have a short half-life. Now a day the controlled drug delivery system is themost popular system of the drug delivery which minimize the risk of toxicity bymaintaining the release of drug from its dosage form and target sitespecificity of the formulation.

Interpenetrating polymer network (IPN) are alsomost popular and rising biomaterial for the novel drug delivery. An IPN is a simple structure of two or more polymersin which they are combined partially with each other by a bonding between them. the bond is not too strong we can say that the bonding between the polymers arenot covalent. The bond between polymer in IPN can be easily broken when it comecontact with a solvent medium or

chemical. The formation of IPN is happened by the combination of two polymerat a specific temperature so the phase separation is impossible at thatcondition at the normal temperature or it can be happened by the influence ofanother chemical or solventThe properties of both the polymer used in IPN arecombined and also can be provide a synergistic effect.

2)Types of IPN-2. 1)-Based on chemical bonding- in these IPN, hydrogels are formed by the crosslinking of covalent bonds when irreversiblechemical links are start forming. The water is absorbed from the linking saidand the drug is release by the diffusion mechanism it is not depend ondissolution. a)-Covalent semi IPN- the covalent semi IPNcontain a single polymer network in which two different type of polymers arecrosslinked. b)-Non-Covalent Full IPN- two separate polymersare independently crosslinked in such type of IPN. c)-Non-Covalent Semi IPN- in such system only onepolymer is cross linked with other. 1. 2)-BASED ON ARRANGEMENT PATTERN-a)-Sequential IPN: In this the firstpolymeric network polymerization is accomplished before the polymerization ofsecond polymeric component.

The polymerization of second polymer is followed bythe first polymers network. b)-Semi IPN: in the semi IPN onlyone polymer is crosslinked where another polymer is just arranged in the linearform. c)-Simultaneous IPN: in simultaneous IPN thenetwork is prepared by a process in which both of the polymer networks arepolymerized simultaneously. d)-Novel IPN: the polymer network isinterlocked least partially on molecular level in which two or more than twonetworks may be involved. Here are not any covalent bod present between themand to separate them we have to brake the chemical bond. 3)Method of preparation of IPN microsphere – 3. 1)-Emulsion

crosslinking method- firstly the polymer is dissolve in distilled water and preparedifferent concentration by stirring.

Then another polymer was dispersed in thefirst polymer solution and stirred until the homogeneous solution may prepared. require amount of drug was dispersed in the polymer solution. The drug loadedpolymer solution was emulsified to form water-in-oil (W/O) emulsion using ahigh-speed stirrer in a beaker and add the crosslinking agent on it.

Then washthe prepared microsphere and dried them at 40°C and store them for characterization. 3. 2)-Suspension polymerization method-Different ratio of polymers were dissolve together in deionizedwater. the Ph value of the water phase was adjusted to 4. 0 using HCL solutionand then the water phase was then dispersed into oil phase at 140rpm for30min.

the course emulsion was pressed through a micro-porous membrane under acertain nitrogen pressure, and this preliminary emulsified emulsion was passedthrough the same membrane in the next pass. the obtained emulsion was bubbledwith nitrogen gas to remove oxygen before polymerization. the system was keptat 20°C under a nitrogen atmosphere for 4h. after polymerization thedispersions were washed with acetone and deionized water three times to ensurethe complete removal of unreacted chemicals. the obtained microspheres weredispersed in deionized water for further analysis.

4)Characterization of IPN microsphere- 4. 1)-FTIR-FTIR spectra ismeasured were by using FTIR Spectrometer to confirm the formation of IPNstructure, presence of crosslinking agent in polymer and also to find chemicalstability

of drug in microspheres. 4. 2)-Optical microscopy study-Opticalmicroscope imaging was done by use of optic microscope. 4.

3)-Swelling study-Theswelling efficiency of the crosslinked empty IPN microspheres was determined bymeasuring gravimetrically the extent of their swelling in checked in pH 7. 4buffer solution at 37°C. 4. 4)-Entrapment Efficiency-the entrapmentEfficiency was analysed by using a UV spectrophotometer at the specificwavelength. 5. 5)-Differential Scanning Calorimetric (DSC) studies-Differential scanning calorimetric curves were recorded on a TAinstruments 5.

6)-X-Ray Diffractions (X-RD) studies-X-RD measurement of raw drug, drug-loaded microspheres andplain microspheres were recorded. 6. 7)-Particle Size and Scanning Electron Microscopic (SEM) studies-The results of particle size of microspheres were determine withthe help of SEM. 6. 8)-In-vitro drug release-IN-vitrodrug release from IPN microspheres was studied at pH 1.

2 HCL solution 6. 8 and7. 4 phosphate buffer solution at 37°C on dissolution apparatus and analyse thesample of each solution at specific time intervals. 5)Benefits of IPN-· The formation of IPN is happened by thecombination of two polymer at a specific temperature so the phase separation isimpossible at that condition at the normal temperature or it can be happened bythe influence of another chemical or solvent which make it a noble drugdelivery system for oral route.· IPN increase the mechanical propertiesand stability of the dosage form.

· As long as the reacting ingredients areblended thoroughly during the synthesis, thermodynamic incompatibility isovercome due to the permanent

interlocking of the network segments.· When the blends are subjected to stress, they can keep the separate phases together.· Due to the infinite zero-viscosity ofthe gel phase separation between the component polymers is almost impossible. 6)Objective of the study- 7)Polymer profile- Isabgol- Isabgol is an important medicinal cropof India. It is a stemless herb. The husk is the rosy? white membranous covering of the seed, which constitutes the drug, mainly given as a safe laxative, particularlybeneficial in habitual constipation, chronic diarrhoea and dysentery.

It is a100% natural product. It is a soluble fibre (is viscous and forms gel inwater). The soluble fibre comes from the dried husk of the psyllium seed.

Thatis, psyllium husk is the cleaned dried outer coating of the Psyllium Seed. Recentinterest in psyllium has arisen primarily due to its use in high fibrebreakfast cereals and from claims that these high fibre cereals containingpsyllium are effective in reducing cholesterol. Several studies point to acholesterol reduction attributed to a diet that includes dietary fibre such aspsyllium. Research reported in The American Journal of Clinical Nutritionconcludes that the use of soluble? fibre cereals is an effective and well tolerated part of a prudentdiet for the treatment of mild to moderate hypercholesterolemia.

Research alsoindicates that psyllium incorporated into food products is more effective atreducing blood glucose response than use of a soluble fibre supplement that isseparate from the food. Although the cholesterol reducing properties and glycaemicresponse properties of psyllium containing foods are fairly well documented, the effect of long term inclusion of psyllium in

the diet has not beendetermined. Cases of allergic reaction to psyllium containing cereal have beendocumented. 5Psyllium mucilage possesses several other desirable properties. As a thickener, it has been used in ice cream and frozen desserts. A 1.

5%weight/volume ratio of psyllium mucilage exhibits binding properties that aresuperior to a 10% weight/volume ratio of starch mucilage. The viscosity ofpsyllium mucilage dispersions is relatively unaffected between temperatures of68 to 122°F, by pH from 2 to 10 and by salt (sodium chloride) concentrations upto 0. 15 M. These properties in combination with psyllium’s natural fibrecharacteristic may lead to increased use by the food processing industry. Technical grade psyllium has been used as a hydrocolloidal agent to improvewater retention for newly seeded grass areas and to improve transplantingsuccess with woody plants. PVA(poly-vinyl-alcohol)-Polyvinyl alcohol is an odourless and tasteless, translucent, white or cream colouredgranular powder. It isused asa moisture barrier film for food supplement tablets and for foods that containinclusions or dry foodwithinclusions that need to be protected from moisture uptake. Due to theirsimple structure and unique properties such as adhesiveness, strength, filmforming, biocompatibility, swelling, safety, and non-carcinogenicity, PVOHpolymers have found applications in different industries including textile, paper, adhesives, food, biomedical and pharmaceutical in particular.

Glyceraldehyde- Glyceraldehyde is a triosemonosaccharide with chemical formula C? H? O?. It is the simplest of all common aldoses. Itis a sweet, colourless, crystalline solid that is an intermediate compound incarbohydrate metabolism. DL-Glyceraldehyde is also used as crosslinking agentin the

preparation of various type of microsphere. 8)Drug profile-Diclofenac Sodium-Diclofenac Sodium is prototypical NSAID, a phenyl acetic acidderivative structurally related to meclofenamate sodium and mefenamicacid that was developed specifically as an anti-inflammatory agent.

Chemical Formula- C14H10Cl2NO2. Na IUPAC Name- 2-(2-(2, 6-dichlorophenylamino) phenyl) acetic acid, sodium. Synonym- 2-(2, 6-Dichlorophenyl)-amino-benzeneaceticAcid, Sodium Average Molecular Weight- 318. 1 Melting Range- 281-284°C Standards- Diclofenac Sodiumcontains not less than 99. 0% and not more than 101. 0%ofdiclofenac sodium.

Loss on Drying- Not more than0. 5% of its weight Packaging and Storage- Preservein light resistant containers, and store at controlledroomtemperature. Pharmacokinetics-AbsorptionBioavailability: It iswell absorbed following oral administration. It undergoes first-passmetabolism; only 50–60% of a dose reaches systemic circulation as unchanged drug. Peakplasma concentration usually attained within about 2 hours. Onset: Single 50- or100-mg doses of diclofenac potassium provide pain relief within 30minutes. Duration: Painrelief lasts up to 8 hours following administration of single 50- or 100-mgdoses ofdiclofenac sodium.

DistributionExtent: Following oraladministration, concentrations in synovial fluid may exceed thoseinplasma. Plasma Protein Binding: > 99%. EliminationMetabolism: Metabolized in theliver via hydroxylation and conjugation. Somemetabolitesmay exhibit anti-inflammatory

activity. Elimination Route: Excretedin urine (65%) and in feces via biliary elimination (35%) asMetabolites Half-life: Oralpreparations: 1–2 hours. Pharmacodynamic-Drug Category- Anti-Inflammatory Agents, Non-Steroidal Inhibits cyclooxygenase-1 (COX-1) and COX-2s Nonsteroidal Anti-inflammatory Agents (NSAIDs) Pharmacology: Diclofenachas analgesic, antipyretic and anti-inflammatory activities. Itspotencyagainst cyclooxygenase-1 (COX-1) and COX-2s is substantially greater than thatofseveral other NSAIDs. Diclofenac is used to treat pain, dysmenorrhea, ocularinflammation, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and actinickeratosis.

Mechanism of Action: Theexact mechanism of action is not entirely known, but it isthoughtthat the primary mechanism responsible for its anti-inflammatory, antipyretic, andanalgesic action is inhibition of prostaglandin synthesis by inhibition ofcyclooxygenase(COX). It also appears to exhibit bacteriostatic activity by inhibitingbacterialDNA synthesis. Inhibitionof COX also decreases prostaglandins in the epithelium of the stomach, makingit more sensitive to corrosion by gastric acid.

This is also the mainside-effect ofdiclofenac. Adverse Reactions: Oral diclofenac: abdominal pain or cramps, constipation, diarrhea, flatulence, GIbleeding, GI perforation, peptic ulcer, vomiting, dyspepsia, nausea, dizzinessheadache, liver function test abnormalities, renal function abnormalities, anaemia, prolongedbleeding time, pruritus, rash, tinnitus, edema. CardiovascularSystem: congestive heart failure, hypertension, tachycardia, syncope. DigestiveSystem: dry mouth, esophagitis, gastric/peptic ulcers, gastritis, jaundice. NervousSystem: anxiety, asthenia,

confusion, depression, drowsiness, Insomnia, malaise, nervousness, tremors, vertigo. RespiratorySystem: asthma, dyspnoea. Uses – Orally for symptomatic management of primarydysmenorrhea. For relief of mild to moderate pain.

For relief of the signs and symptoms ofsymptomatic treatment of osteoarthritis rheumatoid arthritis and ankylosingspondylitis. For relief of the signs and symptoms ofrheumatoid arthritis. 9)Literature review-Ø Kurkuri M.

D., and Aminabhavi T. M. find in their study about Polyvinyl alcohol and poly acrylic acid sequential interpenetrating networkpH-sensitive microspheres for the delivery of diclofenac sodium to theintestine that the release of drug from microgels was dependent upon the pH ofthe medium, extent of crosslinking and the amount of drug loading. Ø Sekhar E. C.

, Rao K. S. V. K.

and Raju R. R. find in their study aboutChitosan/guargum-g-acrylamide semi IPN microspheres for controlled releasestudies of 5-Fluorouracil” that the SEM shows the semi IPNMs was spherical with size around 200µm and theencapsulation efficiency of drug was achieved 58%. Ø Banergee S.

, Chaurasia G, Pal D., Ghosh A. K.

, Ghosh A. and KaityS. studied on investigation on crosslinking density for development of novelinterpenetrating polymer network based formulation and find that in SEM theshape of microsphere was spherical and they come on a point that the novelformulation can be a potential carrier for controlled delivery of short halflived drugs. Ø Sharma V. K., Mazumder B.

find in their study about Crosslinking ofIsabgol husk polysaccharides for microspheres development and its impact onparticle size, swelling kinetics and thermal behaviour" that the microsphereobtained from emulsification method was spherical and free flowing. Ø Lai. E., Wang Y. , Wei Y and Li G. study about Preparation ofUniform-Sized and Dual Stimuli-Responsive Microspheres of Poly(NIsopropylacrylamide)/Poly(Acrylic acid) with Semi-IPN Structure by One-StepMethod" and was find that the prepared semi-IPN microspheres could respondindependently to both pH and temperature changes. Ø Bhardwaj V.

, Harlt G. and Kumar S. find in their study aboutInterpenetrating Polymer Network (IPN): Novel Approach in Drug Delivery thatthe excellent physicochemical attributes such as providing stability to theformulation, improve solubility of hydrophobic drugs, exilent swelling capacityand its biodegradability , drug taegeting in a specific tissue and very weakantigenicity was made IPN the primary resource in pharmaceutical and medicalapplication. Ø Kulkarni P. andKeshavayya J. find in their study about chitosan-sodium alginate biodegradable interpenetrating polymer network beds for delivery of ofloxacinhydrochloride" that the encapsulation efficiency was varied between 76 to 86%. Ø Angadi S.

C., Manjeshwar L. S., Aminabhavi T. M. find in their studyabout Interpenetrating polymer network blend microspheres of chitosan and hydroxyethylcellulose for controlled release of isoniazid" that the drug loadedmicrospheres was find in the spherical shape with entrapment solution efficacyfrom 50 to 66 %. Ø Shivashankar M.

and Mandal B. K. find in their study on a review ofinterpenetrating polymer network” that the limitation in the natural andsynthetic polymer was overcome by the physical and chemical alteration ofpolymer by interpenetrating polymer network. Ø Angadi S. C., Manjeshwar L.

S., Aminabhavi T. M. find in their studyabout Stearic Acid-Coated Chitosan-Based Interpenetrating Polymer NetworkMicrospheres Controlled Release Characteristics that the coted microsphere wasfind in the range of 502nm to 52 µm and the encapsulation efficiencies was65-78%. Ø Kodavaty J ad Deshpande A. P. find in their study about Mechanicaland Swelling Properties of Poly vinyl alcohol and Hyaluronic Acid Gels used inBiomaterial Systems – a Comparative Study that the gel strength was decreseswith increase in collagen content due to the effect of collagen on ineffectivecrosslinking of PVA molecules in the presence of collagen during the formationof interpenetrating network. Ø Muppalaneni S.

and Omidian H. find in their study about Polyvinyl Alcohol in Medicine and Pharmacy: A Perspective” that Both chemically and physically-modified PVOH structures have foundapplications in biomedical and pharmaceutical area. Ø Angadi S. C., Manjeshwar L. S., Aminabhavi T. M.

find in their studyabout novel composite blend microbeads of sodium alginate coated with chitosanfor controlled release of amoxicilline that the size distribution of beadsloaded with drug was find in the range of 745-889µmand the encapsulation efficiencies was find 52 to 92%. Ø Gaaz T. S. , Sulong A.

B., Akhtar M. N., Kadhum A. A. H., Mohamad A. B.

and Al-Amietry A. A. on their study about Properties and Applications ofPolyvinyl Alcohol, Halloysite Nanotubes and Their Nanocomposites” was that PVAis applicable due to their biocompatibility, non-toxicity, no carcinogenicity, smoothness and flexibility in potentialapplication in drug delivery systems. Ø Kokardekar R. R.

, Chaudhari Y. S., Kumavat S. D. and Pawar H.

A. find intheir study about Developmentand Evaluation of Sustained Release Microspheres of Glibenclamide by EmulsionSolvent Evaporation Method” that the microspheres were spherical andporous in nature. Ø Patel N. R., Patel D. A. , Bhradia P. D.

, Pandya V. and Modi Darshanfind in their study about microsphere as a noble drug delivery that themicrosphere was a better choice for the sustained drug delivery system. Ø Jain N. Banic A.

and Gupta A. study about Noval interpenetratingpolymer network of lepidium sativum and poly vinyl alcohol for the controlledrelease of simvastatin” that the microsphere found was spherical with smooth surface and the drug entrapmentefficiency was find upto 86. 65%. Ø Dinarvand R., Mahmoodi S., Farbound E., Salehi M. and Atyabi F.

find in their study about Preparation of gelatine microspheres containinglactic acid effect of cross-linking on drug release that Microspheres prepared with a larger amount ofcross-linking agent, or after longer cross-linking time was showed a reducedswelling ratio in aqueous media. Ø Torres M. T., Vieira R. S., Beppu M. M.

, Arruda E. J. and Santana C. C. study about Production of Chemically Modified Chitosan Microspheres by aSpraying and Coagulation Method” and find that The microspheres was presenteda fairly good sphericity but an irregular micro-surface morphology. Ø Dinarvand R.

, Rahmani E. and Farod E. find in their study aboutGelatin Microspheres for the Controlled Release of All-Trans-Retinoic AcidTopical Formulation and Drug Delivery Evaluation” that the drug was releasedfrom the cream formulation followed zero order release profile. Ø Pandey N.

, Dr. Sah A. S, Mahra K.

find in their study aboutFormulation and evaluation of floating microsphere’s of nateglinide” that thedeveloped floating microspheres of nateglinide was offers a suitable andpractical approach for prolonged release of drug over an extended period oftime and thus oral bioavailability, efficacy and patient compliance isimproved. Ø SekharE. C., Rao K.

S. V. K., Rao K. M. S. and Raju R.

R. study about Development of Gelatin-Lignosulfonicacid Blend Microspheres for Controlled Release of an Anti-Malarial DrugPyronaridine” that Both encapsulation efficiency and release patterns wasfound to be dependent on the nature of the cross-linking agent as well asamount of drug loading. 10)Methodology-