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A Review on Preparation of Poly -N -Vinyl Pyrrolidone Oxime and study of its Structural and Physicochemical properties

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Abstract

Poly-N-Vinyl Pyrrolidone (PVP) with molecular formula $(C_6H_9NO)_x$, of molecular weight 40,000 is a water soluble polymer, is a highly biocompatible polyactamide homopolymer. PVP is taken as an important component is firstly converted into it oxime derivative. PVP is treated with hydroxylamine hydrochloride ($NH_2OH.HCl$) in alkaline medium to facilitate smooth reaction. Spectroscopic characterization of the PVP-Oxime molecule is carried by Fourier Transmission IR Spectra, ^1H NMR Spectra, UV-VIS Spectrophotometer. The IR vibration frequencies of PVP-Oxime show the presence of side chains as poly vinyl chain. ^1H NMR Spectra infers the presence of oxime group in the molecule. At 0.001% concentration of PVP-Oxime absorbance of UV-Vis spectra is studied. Physico-chemical characterization of the PVP-Oxime molecule is studied by sophisticated Analytical instrument Survismeter. It includes Viscosity, Surface tension, Friccohesity, interaction between the molecules, volumetric interaction in bulk and in thin films. The 0.001%, 0.0005%, 0.00025%, 0.000125%, 0.0000625% samples of different concentration of PVP-Oxime in aqueous media are studied for adhesive, cohesive, frictional forces, Wetting and De-wetting effects. The supramolecule can be extensively applied as an adsorbent surfaces for many bio-physicochemical phenomena. The surface morphology of the Poly-N-Vinyl Pyrrolidone and its Oxime molecules are studied by Scanning Electron Microscopy (SEM) techniques. The porosity and the nanostructure surface properties of the molecule can be studied. Thus the physico-chemical and structural Characterization of the PVP and PVP-Oxime nano particles reveals us the Physical, Chemical and biological activities of the molecule making it more applicable in broad areas of medicinal chemistry, Bio-physical Engineering, Drug chemistry as nano bio-chips, biosensors, drug loading and drug delivery systems, etc.

Keywords: PVP-Oxime, adsorbent, wetting effects, biological activities, nanostructures, biosensors

Introduction

Nature has created the world with large biodiversity among living organisms, with limited number of building blocks-carbohydrates, amino acids, lipids, nuclei acids, which has various bio-chemical diversities. These assemble in different ways which enables us to study a wide range of possible supramolecular structures. Latest and current research scenario demands focus on the small organic molecules which have proven to be invaluable tools for

investigating biological systems, but there is still much to learn from their use. To discover and to use more effecient new chemical tools to understand biology, strategies are needed that allow us to systematically explore 'biological-activity space'. Such strategies are helpful in analysing both protein binding of, and phenotypic responses to, small organic molecules. The advanes in synthetic chemistry and biotechnology enables us to synthesise new biomaterials uing these smaller organic molecules as building blocks that have not been yet made. Those methods which promise to shorten the time or the cost are eagerly taken up, and this is with combinatorial chemistry and multiple parallel syntheses. Such self assembled materials can be improved with enhancing their properties as well as their applications in drug chemistry [1-3]. Combinatorial chemistry is the collection of systemic and repetitive covalent connection of variety of building blocks of varying structures leading to the formation of new diverse supramolecular entities which is the recent trend in the pharmacogenics.

Solid phase synthesis and solid phase organic synthesis can be used. The use of central core molecule with multiple binding sites as a template for the construction of libraries has been reported by Carell and co-workers [4]. The application of parallel synthesis to lead optimization programs in drug discovery has been an ongoing challenge [5]. In addition to the potential for targeting, the physicochemical properties of nanoparticles make them ideal devices for the delivery of compounds to tumor cells. Molecules such as contrast agents or drugs can be loaded into the core of a nanoparticle or applied as a coating to its surface. The process of a single nanoparticle carrying a large number of drug molecules or ions is referred to as "nanoparticle amplification" and explains the concept of nanoparticles as delivery devices[6]. In the mordern research nanoparticles are finding increased uses in drug delivery applications as a means to increase treatment efficacy and improve patient care. Engineered polymeric nanoparticles that undergo a hydrophobic to hydrophilic transition at a definite pH range afford swelling and rapid release of their contents has been reported [7]. Polymeric systems play a very important role in industrial and chemical processes as well as in biological processes of living organisms. A novel magnetic drug-targeting carrier characterized by a polymeric core - shell structure has become a matter of interest in the clinical chemistry [8-9]. So, polymeric systems has become a matter of great interest for biochemists and chemical engineers as it offers chemical, mechanical and thermal robustness, adhesion to a wide variety of materials like different polymers, inorganic metals etc. polymeric systems can be processed into thin films, fibres, wave guides, and large areas structures, optical sources and detectors integration with electronic systems, low cost and potential for long range orientation [10-11]. Recent trends in nano particle sized bio- physical engineering has widely increased the formulation opportunities of water-insoluble drugs. Thus, these studies could serve as a basis for the use of nanoparticle-mediated drug delivery to enhance bioavailability and limit any unwanted toxicity of chemopreventive agents. Combination of different classes of materials may lead to the formation of our new products which are of desired features and properties and can fulfill our objectives [12-15]. High molecular weight polymers have been widely used as soluble drug carriers to improve drug targeting and chemotherapeutic efficacy. Dendritic polymers have broad range of applications

as monodisperse drug carriers due to their well-defined structure, multivalency, and flexibility for tailored functionalization [16]. A variety of approaches have been made in which drugs have been conjugated to polymers to improve their water solubility properties, to decrease their toxicity due to local accumulation of the drug prior to reaching the target tissue, and to protect them from any possible enzymatic degradation or hydrolysis within the biological system. By manipulating the chemical composition of the dendritic systems the biocompatibility and pharmacodynamics can be tuned desirably [17].

Poly-N-Vinyl Pyrrolidone (PVP):
Polyvinylpyrrolidone is a white, light, flaky powder, water soluble photopolymer readily absorbs up to 40% of its weight in atmospheric water. PVP is a nonionic water-soluble polymer, is readily soluble in polar solvents such as alcohols, amines, acids and chlorinated hydrocarbons.

Technical Applications:
Polymer PVP was used as a blood plasma expander for trauma victims. It is used as a binder in many pharmaceutical tablets and forms a complex with iodine called povidone – iodine complex used a disinfectant.

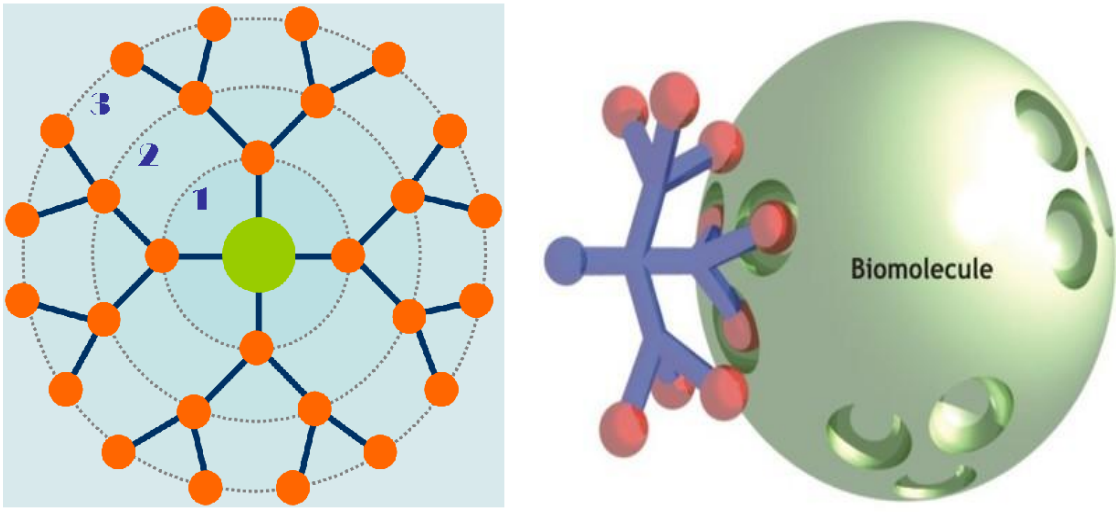
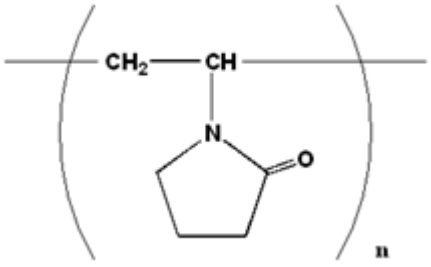


Fig. 1: Dendritic System and Dendrimer Surfaces to Bind Biological Molecules.



Polyvinylpyrrolidone (PVP)

PVP is used as stabilizer in food additive.PVP can be used as substitute to blood plasma with no side effects.The tensile strength of the hydrogel membranes increases with increasing PVP ratios. The prepared hydrogel membranes were found to be biocompatible with B16 melanoma cells. There is a decrease in crystallinity of the hydrogel membranes with increase in PVP ratio. A medium containing polyvinylpyrrolidone (PVP), in addition to DMSO, can be used for long-term storage of hepatocytes for preparing primary cultures to be used in drug metabolism studies [18-21]. PVP is hydrophilic in nature and highly biocompatible, and its thin films have found many applications in the biomedical community, one of which is as antibiofouling surfaces [22]. PVP shows good compatibility with plasticizers, hydrophilic binders, and thin films. PVP shows reversible association with iodine, tannins, dyes polyphenols and forms complexes. The inhibitory effects of polyphenolic contamination of RNA are reversed by the inclusion of PVP in the polymerase chain reaction [23]. PVP binds to polar molecules , because of its polar nature. This has made its application in coatings for photo-quality ink-jet papers and transparencies, in inks for inkjet printers. In the immunochemical studies PVP is used as a blocking agent[24]. The change in the properties upon the addition of PVP into the blends prepared with chitosan shows the hydrophilicity of the blends increases due to the presence of PVP in the chitosan substrate which helps in breaking the hydrogen bonds in between chitosan molecules and causes the blends to swell.

Pharmaceutical Applications of PVP:

The effects of two typical additives, lithium chloride (LiCl) and glycerol, on the fabrication of poly (vinylidene fluoride-co-hexafluropropylene) (PVDF-HFP) asymmetric microporous hollow fiber membranes were studied by Lei Shi in terms of membrane morphology, structure, and permeation performance, hydrophobic and mechanical property in which the membrane hydrophobicity was affected more by PVP, by changing the thermodynamic and kinetic properties.

Fig. 2: Adhesive applications of PVP.

The combined effect of hydroxypropyl-β-cyclodextrin (HPβCD) and polyvinylpyrrolidone (PVP) on the solubility of naproxen (NAP) was studied at different temperatures. Variations in thermodynamic parameters infer the significance of PVP in the formation of a NAP–HPβCD–PVP ternary complex. The combination of PVP and HPβCD has led to a synergistic increasing effect of the aqueous solubility of NAP (120 times that of the pure drug) [25-26]. Using PVP as additive on polyvinylidene fluoride (PVDF), the hollow fibre membrane morphology and structure for microfiltration was studied where the rejection rate and tensile strength was increased. Enrica Fontananova prepared Porous asymmetric hydrophobic membranes were from poly(vinylidenefluoride-co-hexafluoropropylene)and polyvinylidenefluoride (PVDF) homopolymer by the phase inversion process, where the membranes made of PVDF copolymer offer a higher resistance to mass transport is due to lower membrane porosity and pore size[27].To improve the dissolution performance of a drug Bay t3839 Andreas Ohm **[**30**]**applied coprecipitate formulation method and the necessary ratio polyvinylpyrrolidone (PVP) to drug substance was found to achieve supersaturation ,as the drug is highly sparingly soluble drug. PVP and co-polymer product has been developed as a new valuable biosensor and conducting copolymer molecule to serve as useful biochip and a biocompatible template [31]. Water-soluble complexes of AmB (amphotericin B) and polyvinylpyrrolidone (AmB–PVP) compared with PVP display lower cytotoxicity while maintaining antifungal activity was less hemolytic and cytotoxic than AmB [32]. Polyvinylpyrrolidone is one of the most important excipient used in modern pharmaceutical technology. Combination of Ce 6-PVP induced fluorescence imaging and spectroscopy can be widely applied for optical detection and discrimination between cancer and the surrounding normal tissues. Because of the selective localization and photodynamic activity of Ce6-PVP, it is used as a therapeutic agent for photodynamic cancer therapy [33-36].

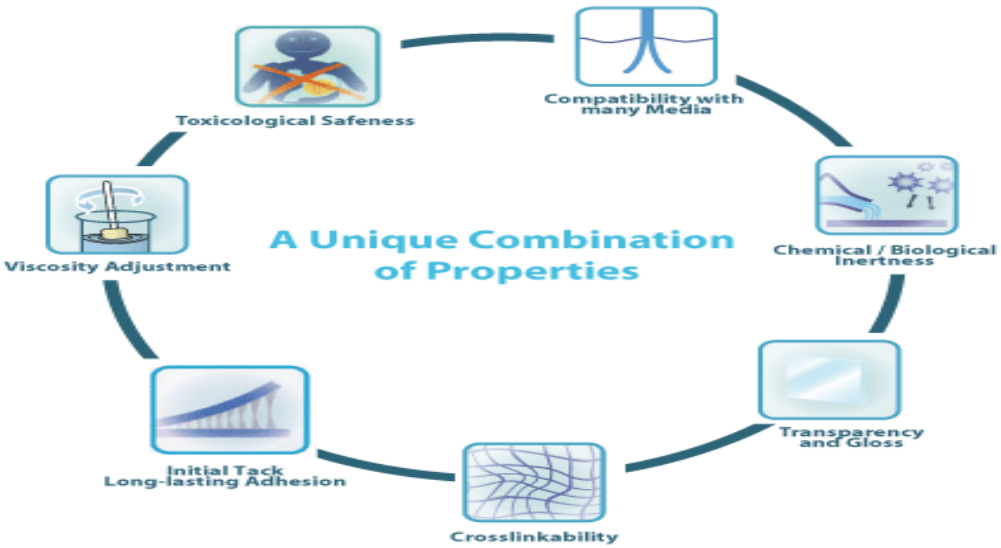


Fig. 3: Properties of PVP.

Industrial applications of PVP:

The sorption and desorption of poly (vinylpyrrolidone)-Se-0 (PVP-Se-0) nanoparticles on gel films of cellulose Acetobacter xylinum (CAX) are studied. Depending upon their sorption inside the cellulose gel film and on the film surface, these nanoclusters differ in the number and size and can be used as cellulose template in medical practices. Nanoscale optical memory and photo fabrication on spin-coated dye-doped PVP polymer films are studied with respect to storage capacity and readout signal-to-noise ratio with near-field one-photon and two-photon excitations. Doped polymer colloids are applied for conductivity were prepared electrochemically which adsorbs calcium, copper and iron ions from aqueous solutions and are used as biosensors. TiO_2 films doped with ZnP- PVP can be used for optical and photo physical studies. Doped metal oxides are used as thin-film optoelectronic devices in presence of the 1-nm- to 3-nm-thick PVP surfactant layer are applicable as organic solar cells. Sawicka .et.al. by the electrospining technique has prepared nanocomposite fibres of urease and PVP and the materials have proved to be good urea biosensors which may find their applications in the different fields of medical diagnosis, environmental and bio- industrial analysis [37-42]. Poly (vinylpyrrolidone) films containing cobalt chloride or iodine form polymeric complexes with electrical conductivities are observed to be very sensitive to environmental humidity. Huixiang Tang et al. prepared gas sensors based on (PVP)-modified ZnO nanoparticles with different molar ratios of Zn^{2+} ions shows fairly gas sensing properties [43-45]. Chengbin Jing et al. prepared CdS-PVP nanocomposite film that shows excellent optical properties exhibited by a nonlinear optical refractive index and a certain absorption coefficient values and are helpful in the production of optical devices with various shapes. The adhesive joint between silica nanoparticles and ultra thin PVP layers (thickness between 3 and 100 nm) was studied with atomic force microscope. The mechanical properties of the system as well as molecular characteristics of the PVP layer are responsible for the pronounced adhesive property. Thus adhesive properties of the thin films can be very much applicable in different biomedical devices.

Using PVP as a binder, water based alumina tapes were fabricated which shows high flexural strength [46-48]. In the presence of poly (vinylpyrrolidone) electron-transfer quenching of tris (2, 2-bipyridine) ruthenium (II) by methylviologen in an aqueous suspension of clay was studied by Norishige Kakegawa et al [49].

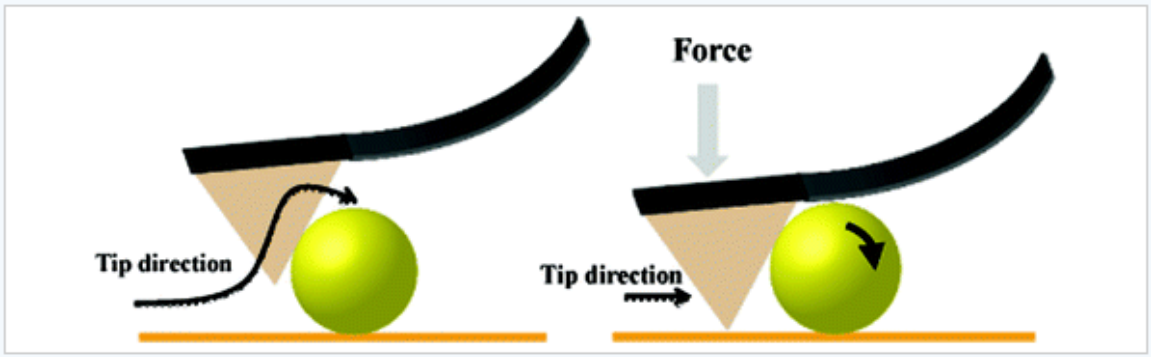


Fig. 4: AFM study of ultra thin PVP layers.

By measuring the corrosion potential, linear polarization resistance and AC impedance during 60 days immersion in NaCl and NaCl + PVP solutions on the corrosion resistance of steel A.A. Gürten et al.[50] observed that the compressive strength of concrete had increased approximately 44% in the specimens containing PVP. PVP-I (povidone) is a potent antiseptic and, when used as a component in a rinse with H_2O_2, it can decrease the level of gingivitis. With regards to patients with adult periodontitis, Dr. Gary Greenstei observations show that PVP-I delivered via an ultrasonic device. Gold nanoclusters are stabilized by poly (*N*-vinyl-2-pyrrolidone) readily oxidize benzylic alcohols to the corresponding aldehydes or carboxylic acids. It is proposed a superoxo-like molecular oxygen species is adsorbed on the surface of the small Au nanoclusters which abstracts a hydrogen atom from the alkoxide. By phase inversion process using immersion–precipitation technique membranes were formed from poly (bisphenol-A sulfone)/poly (vinyl pyrrolidone)/dimethylacetamide/water systems. It explains that the macro voids development is a function of the resistances created by precipitation kinetics of former layers. Polymeric membranes are developed having advanced or novel functions in the various membrane separation processes for liquid and gaseous mixtures (gas separation, reverse osmosis, pervaporation, nanofiltration, ultrafiltration, microfiltration) and in other important applications of membranes such as biomaterials, catalysis (including fuel cell systems) or lab-on-chip technologies[51-54].

Poly-N-Vinyl Pyrrolidone (PVP) Oxime:

The synthesis of Oxime derivative of PVP (Poly-N-Vinyl Pyrrolidone) is carried out by taking PVP (Merck), hydroxylamine hydrochloride (Merck) 1:1 ratio, w/w, followed by the addition of 5ml 1N NaOH solution in 50% ethanolic medium. The reaction mixture was taken in RB flask provided with magnetic stirrer and kept for 20-25 minutes; a white precipitate of PVP-Oxime is formed. The White precipitate formed is filtered through Whatman Filter Paper washing several times with 25% aqueous ethanolic solution. Precipitate formed is Vacuum dried and collected [55-56].

Fig. 5: Advantages of PVP.

Physico - Chemical Characterization:

PVP-Oxime, a derivative of PVP is highly biocompatible and can be applied for broad spectrum of applications. Man Singh et al. has developed a new valuable biosensor and conducting Polyvinylpyrrolidone (PVP)-oximate-silico-benzoyl glycine (POSBG) copolymer molecule to serve as useful biochip and a biocompatible template [57]. The average viscosity and molecular weights ($\bar{M}_v$) of PVP-oxime and the copolymer were determined with their respective dilute aqueous solutions at pH 7. The IR spectra of the PVP-oxime depicts the 1602, 1688 $^{cm-1}$, stretching vibration frequencies noted in the spectra infer the presence of – C = N, – C = O, functional groups, respectively, in the molecule [58]. The presence of colloidal particles or any polymeric solute increases the viscosity of the liquid than that of pure solvent. It was shown by Einstein that the relative viscosity of spherical colloidal particle is given by the expression:

$$\eta_r = \eta / \eta_\circ = 1 + 2.5\theta_2 \qquad (1)$$

η_r = the relative viscosity, η = viscosity of the solution, $\eta_\circ$ = viscosity of the pure solvent, θ_2 = the volume fraction of the colloid particle. According to the above equation the volume or overall size of the colloidal particle of polymer and imbibed solvent increases ,volume fraction θ_2 and the relative viscosity η_r also increases. The η (viscosity) values are the function of the size and shape of the polymeric molecule [59-60]. Viscometric studies can be done by the sophisticated analytical instrument "Survismeter" [61] based on 2 in 1 technique for surface tension and viscosity data measurement. These intrinsic viscosity data has been considered as an effective technique for (M_W) molecular weight determination. 0.001%, 0.0005%, 0.00025%, 0.000125%, 0.0000625% samples of different concentration of PVP-Oxime in aqueous media are studied for adhesive, cohesive, frictional forces, Wetting and De-wetting effects by Survismeter [61-64]. Apart from frictional and cohesive forces a new property known as Friccohesity (σ)[65] which illustrates the rheological behaviour of the biological fluids and the diffusion of the biocompatible ions Na^+ , K^+, Mg^{2+} etc. and other molecular ions, Zwitter ions (amino acids), globular polyvalent protein ions get transported with biofluids in the blood capillaries. Depending upon the fluid behaviour fluids are categorized as: Time independent Non - Newtonian Fluids and time dependent Non - Newtonian Fluids [66]. Property of some non - Newtonian pseudo plastic fluids show a time dependent change in viscosity is known as Thixotropy.

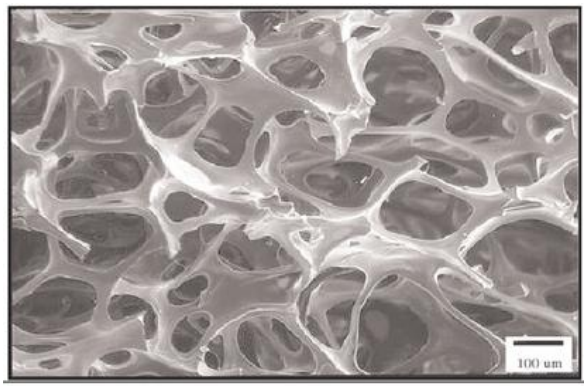


Fig. 6: SEM picture of PVP hydrogel.

Different formulations based on bioadhesive and biocompatible polymers with different rheological properties in terms of flow and oscillation properties are widely employed as important parameters for the application as OVD(ophthalmic viscosurgical devices)[67-68].The study of rheological properties of biological fluids are important tools for correlating the pathological conditions with the rheological behaviour and biosubstitutes[69]. The wetting and

dewetting properties of thin films of polymer of PVP-O can be studied by the relation $\eta h^2 / t$ vs. γ. Bulk surface tension measurements of the polymer cannot be used to estimate the stability of ultra thin films. Polymer film wettability is also influenced by, the interfacial free energy between the polymer and the substrate [70]. Surface morphology of the molecule is studied by Scanning Electron Microscopy. Controlling the size, shape, and structure of polymer nanoparticles is technologically important because of the strong correlation between these parameters and drug loading, drug delivery, optical, electrical, and catalytic properties etc. To prepare pulsatile release formulations consisting of two-layered tablets appropriate for preventing ischemic heart diseases, PVP/HPMC miscible blends with enhanced mucoadhesive properties were taken. The active core was constituted by a FELO/PVP 10/90 w/w solid dispersion while for the adjustment of the drug release time the coating layer was composed of PVP/HPMC blends at different compositions, which acts as a stimulus responsible layer [71]. γ-Butyrolactam is manufactured conventionally by the reaction of butyrolactone (derived from 1,4-butanediol) with ammonia and is used as a precursor for the manufacture of poly(vinylpyrrolidone).Poly (vinylpyrrolidone) is a specialty polymer with applications as binders and blood plasma substitutes in the cosmetic and medical sectors. The scope of the possibilities to generate current functionalized chemical materials using amino acids from biomass instead of fossil resources, thereby taking advantage of the biomass structure in a more efficient way for the production of fuels or electricity[72]. It was reported that polyvinylpyrrolidone (PVP)-iodine complex (PVP- iodine) gradually released active iodine and the broad-spectrum microbicidal activity of the iodine, electrospun PVP-iodine nanofibers can have external anti-bacterial, antimycotic and antiviral applications. The detection of interactions between a photosensitizer, hypericin (HY), and its solvent system prepared with a formulation additive, polyvinylpyrrolidone (PVP), a commonly used pharmaceutical excipient has been reported. The results reveal out the coordination of HY-PVP binding, HY disaggregation in the presence of PVP, and strengthened HY tumor uptake selectivity. Thus PVP is suggested as a potential adjuvant to previously investigated N-methyl pyrrolidone (NMP) in the HY delivery system as well as a replacement for the conventionally used albumin in the HY bladder instillation fluids preparation for clinical use[73-74]. A new series of poly(vinyl pyrrolidone) (PVP) and silver chloride nanoparticles (AgCl) composite fibres as been synthesized by Jie Bai et al. which can be used in a wide range owing to their unique properties and intriguing applications in many areas[75- 76].

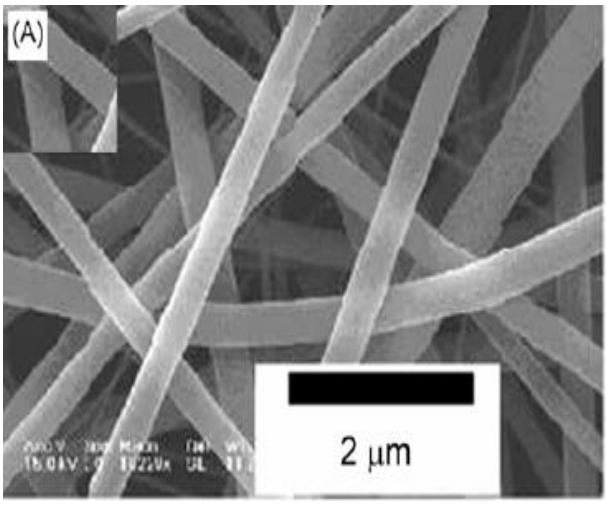


Fig. 7: SEM images of pure PVP nanofibres.

Conclusions

This review has covered the diverse applications of PVP and its derivative PVP-Oxime. The review is by no means is exhaustive, and new applications are emerging out continuously using PVP. The above studies reveal that PVP and its derivative PVP-Oxime are highly biocompatible. The interaction of PVP-Oxime with water is very high which shows the presence of free sites available in the molecule for binding. Thus, the very own prepared molecule can be applied widely for various biomedical applications as drug vehicles, drug carriers, chemical sensors etc.The above studies infer that the PVP and PVP derivatives are promising materials for controlled drug delivery systems. Coatings made from PVP has been accepted by medical communities because of their high biocompatibility, antithrombogenecity, protein repelling property, commercial availability etc.The presence of hydrophilic and hydrophobic functional groups on the PVP and PVP-Oxime molecules and the nanoparticle size makes the molecule ensuring for its accessibility to all the interior sites within the biological systems and thus can be very useful in the drug delivery systems as carriers and vehicles. Hydrogels of PVP and its derivatives are extensively used as substitutes for the vitreous humor of the eye and also in the tissue engineering and tissue regeneration. The rheological properties of thin films of the polymer are widely used as an important parameter for its application in various surgical instruments. The friccohesity, cohesive and adhesive forces, wetting and dewetting effects of the PVP-Oxime molecule can be studied from this review thereby making the molecule applicable various biomedical and clinical areas. The polymeric molecules have the interfacial energies and physical properties like surface tension, viscosity , frictional forces, pseudo plastic , dilatant behaviour etc.are the important parameters to study the chemical and physical behaviour of the molecule. This review has mainly emphasized on the study of various properties of the PVP and PVP-Oxime molecules which can be applied in the broad spectrum of pharmacogenomics mainly as thin film coatings, chemical biosensors, bio – organic chips, drug loading and drug delivery systems, substitute to biological fluids etc. Polymeric particles are used for the controlled delivery of several types of medicaments, including anticancer agents, antihypertensive agents, immunomodulatory drugs, hormones, vitamins and macromolecules such as nucleic acid, proteins, peptides, antibodies, etc.

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