# Modification of Polyvinylpyrrolidinon With 4-Aminoantipyrine

## As Drug Polymer

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**Abstract:-**

In this work a new drug polymer was prepared from reaction of PVP with 4-aminoantipyrine as antibiotic in 10:1 dioxane :DMF solvent mixture. The prepared drug polymer was formed with 72% conversion percentage.

The physical properties were studied and intrinsic viscosity was equal to 0.83 dl/g. The drug polymer was characterized by FTIR and UV. Spectroscopy. The swelling % were studied in different non solvents. The C,H,N analysis and T.G were analyzed.

The controlled release rates for drug polymer were studied in different pH value at $30C^0$ for 4days. The softening point of the prepared 4-aminoantipyrine drug polymer was 212-220 $C^0$.

**Introduction:**

4-aminoantipyrine(AAP) is a metabolite of aminophenazone and is an aromatic substance with analgesic, anti-inflammatory and antipyretic properties. Although today AAP is scarcely administered as analgesic because of the risk of agranulocytosis [1], it is mostly used as a reagent for biochemical reactions producing peroxides or phenol[2,3] and is also be used to detecting phenols in environment[4]. Due to AAP is widely used in biochemical experiment and in environmental monitoring, AAP as an aromatic pollutant exposes in the environment.

Poly(N-Vinyl-2-pyrrolidinon) PVP is a white or slightly yellow hygroscopic powder, forming hard clear films. The polymer strongly interacts through dipole-dipole attraction, the melt viscosity of the polymer is there for too high for typical thermoplastic-forming operation. Amphoteric PVP has a positive charge below $pH_1$ and negative charge above $pH_2$ indicating enolization [5]. Aqueous solution are midly acidic ($pH_5$), which may be due to the carboxyl and end groups produced during polymerization with peroxides; enolization of the carbonyl group may also be involved [6,7].

Poly(vinylpyrrolidone) is a water-soluble amphiphilic nontoxic polymercommonly used in a wide range of applications in the pharmaceutical and nutritional area, as well as in cosmetics, personal hygiene, paintings, etc.

However , PVP lacks reactive groups what limits the possibility of adding new functions to the polymer in order to modify its physical and chemical properties, Furthermore, large differences in radical reactivity between 1-vinylpyrrolidin-20ne(VP) and most other monomers lead to compositional drift during copolymerization[8]

**Experimental:**

4-Aminoantipyrine, and all other chemicals were purchased by Sigma-Aldrich , polyvinylpyrrolidinone was obtained from Fluka.

All available chemical reagents were used without any further purification. FTIR spectra were taken on a Shimadizu spectrophotometer. Ultra violet spectra was recorded using Shimadizu UV-VIS recorder over the range500-4000$cm^{-1}$. .C.H.N analysis were determined by analyzer type 1106 Carlo Irba.

**Modification of Polyvinylpyrrolidinon PVP with 4-Aminoantipyrine** (9,10)

A mixture of (4g., 0.036 mole) of PVP and 10:1 Dioxane:DMF were placed in a round bottomed flask equipped with a reflux condenser and a magnetic stirrer, under reflux condition. Then (7.32g., 0.036 mole) of dissolved 4-Aminoantipyrine was added gradually, refluxed for 1hour then left the mixture about 10 hours. The colorless viscous polymer was reprecipitate from 50ml of ethanol, the pure polymer was obtained 72% conversion.

**Controlled Released study (11,12,13)**

A 100mg of modified 4-Aminoantipyrine drug polymer was kept in a cylinder containing 50:50ml of buffer:dioxane and in a water bath at 30C without stirring. A sample from the release medium was periodically withdrawn and analyzed by UV. At 300nm to determine the amount of the released 4-Aminoantipyrine. A calibration curve was constructed with a software built in the computerized UV. Spectrophotometer, the amount mg of the released 4-Aminoantipyrine was determined directly from the software for many days, using the calibration curve in different pH values at 30C.

Swelling Percentage of prepared polymer was studied which equals to 8% in acetone and 10% in hexane, swelling% was calculated according to

$\Delta m = m_1 - m_0 / m_0 \times 100$

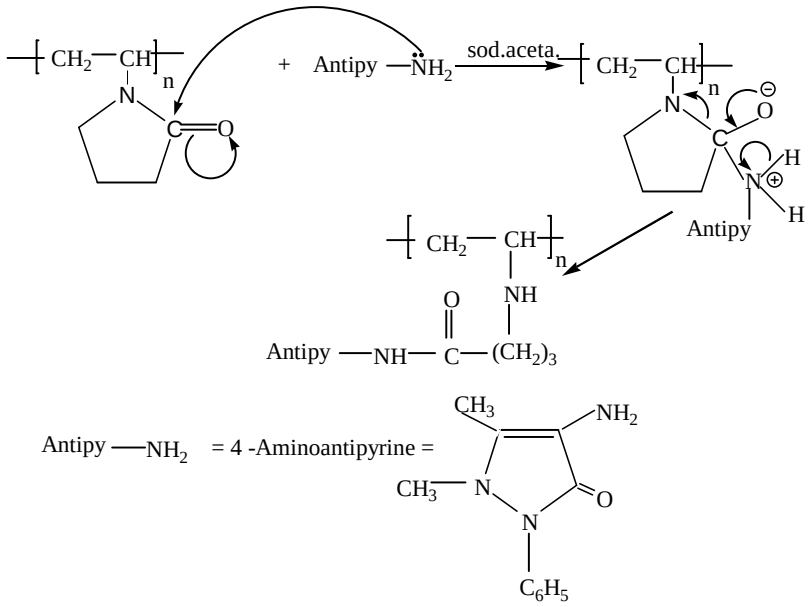
When $m_0$ is the weight of a dry drug polymer

$m_1$ is the swallowed polymer in non solvent

The softening point of the drug polymer was 212-220 $C^0$ which measured by using GallenKamp M.F.B-600 melting point.

**Result and Discussion**

Poly(N-ninyl-2-pyrrolidinone) is a while hygroscopic powder, forming hard clear films. Physical properties are determined on films or powder. The polymer strongly interacts through dipole-dipole attraction. The ring opening reaction of PVP with $-NH_2$ in 4-Aminoantipyrine is illustrated in mechanism below:-



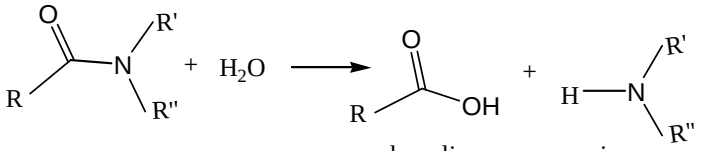

Due to the presence of –NH2 group which is strong nucleophilic attach, the ring opining of pyrrolidinone produced prodrug polymer. The polvinypyrrolidinon connected with amide 4-Aminoantipyrine moiety affords both protection and specific transport properties with longer acting release with higher reactivity in suitable site and this type of drug polymer which hydrolysis in fabrications conditions to delivery of agents, for therapeutic against disceases state. And sustained rate, targeted delivery of drugs and to minimize toxicity and enhanced selectivity.

The structural characterization was done by FTIR spectrum Fig.(2) showed peaks at 3354cm$^{-1}$ and 3367cm$^{-1}$ assigned to –NH-stretching and 1633cm$^{-1}$ assigned to C=O stretching of amide, and 3055cm$^{-1}$ was attributed to C-H stretching of aromatic ring, and peaks at 2636cm$^{-1}$ assigned to aliphatic C-H stretching ;on the other hand, the FTIR showed peaks at 1460,1492 and 1541cm$^{-1}$ due to C=O stretching of the aromatic ring of 4-Aminoantipyrine, the

FTIR of drug polymer which compared with Fig.(1) of FTIR spectra of PVP.

The physical properties of prepared 4-Aminoantipyrine polymer were studied such as intrinsic viscosity which was measured at $30C^0$ with Ostwald viscometer by using dioxane as a solvent.($\zeta_{in}$= 0.83dl/g).

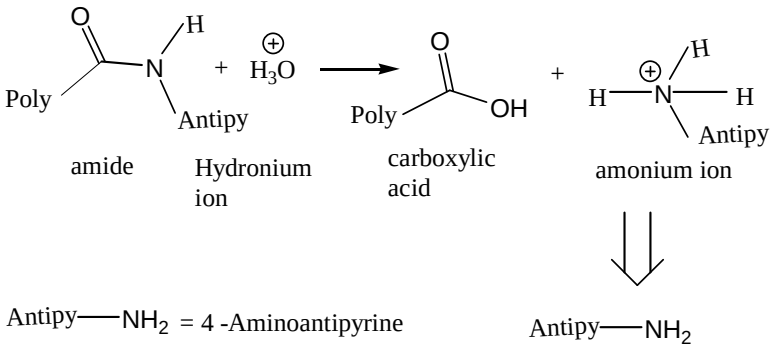
Fig.(3) shows the effects of pH values on the rate of controlled release and profiles of mole fraction of 4-Aminoantipyrine ratio to total moles present in the sample versus time at pH values 4 and 10 at $30C^0$. The only nucleophilic acyl substitution reaction that amides is hydrolysis, Amides are fairly stable in water, but the amide bond is cleaved on the heating in the prescience of strong acid or bases, Norminally this cleavage produces an amine and carboxylic acid.



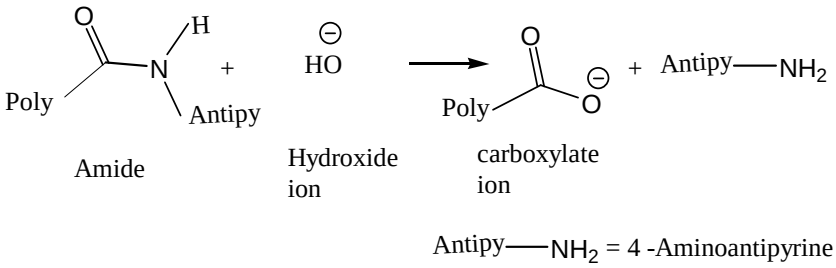

amide water carboxylic acid amine

The release of the drug at suitable condition gradually with outside effect, this hydrolysis of amide group which shown in the following mechanism [14,15]

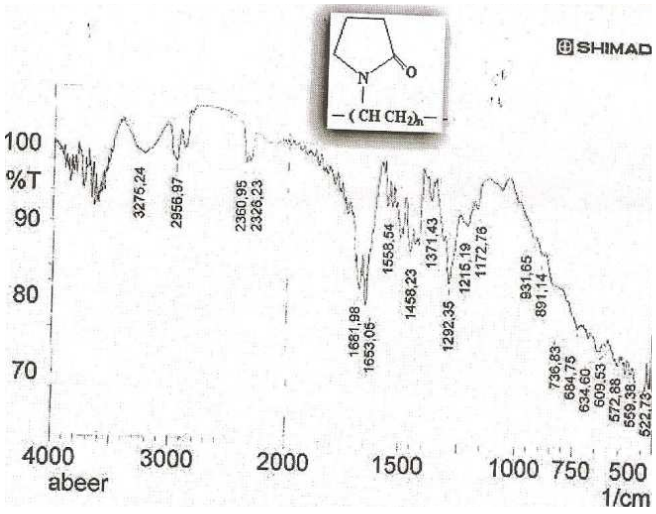
In acid, however, the amine is protonated giving an ammonium ion:-




In base the carboxylic acid is deprotonated, giving a carboxylate ion :-




The purpose of this research was to synthesize polymer based smart bioactive 4-Aminoantipyrine prodrug polymer and one of the main goal in this work is investigation of efficient drug carrier and the effect of pH values on drug release at 30C as illustrated in Fig(3) .


SHIMAD
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1215.19
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931.65
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684.75
634.60
609.53
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1/cm

**Fig.(1) IR spectrum of poly vinylpyrrolidinon**

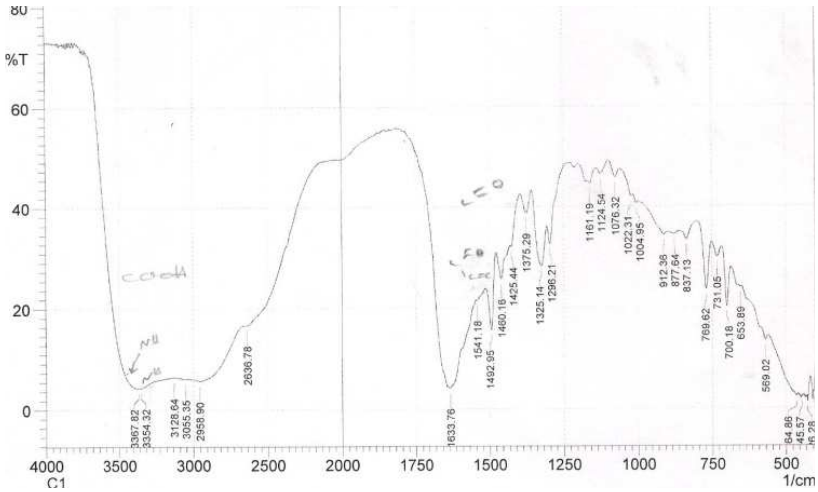
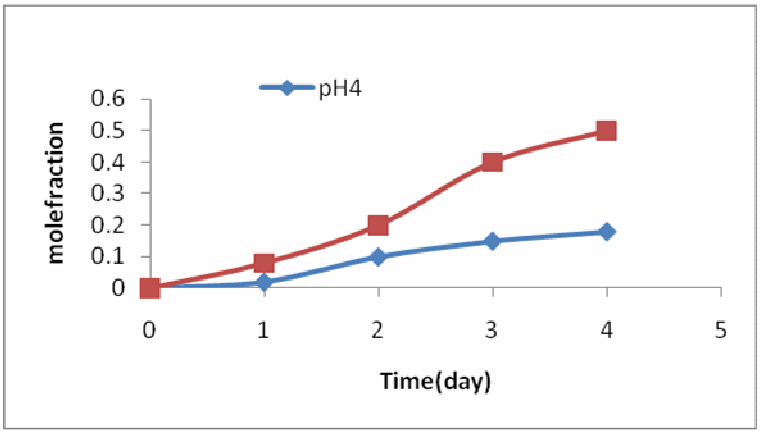



**Fig.(2) IR spectrum of polyvinylpyrrollidinone with 4-Aminoantipyrine**

**(drug polymer)**




**Fig(3) Controlled release drug polymer at 30C$^0$ in different pH**

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