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Physicochemical and antimicrobial studies of polyvinyl alcohol/ chitosan polymer composites comprising low content sulfa drug

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ABSTRACT: Thin-film samples of polyvinyl alcohol (PVA), Chitosan (CS), and their equimass polymeric blend in addition to other samples containing variable content of 2-(4-Hydroxyphenylhydrazono)-N-(4-sulfamoylphenyl)-cyanoacetamide crystal were successfully synthesized. Synthesized samples were examined via traditional spectroscopic techniques including Fourier transforms infrared (FTIR) and UV/visible measurements. Antimicrobial studies against gram-positive, gram-negative, pathogenic yeast were tested for ll studied samples. Obtained data shows a higher activity index for samples with higher drug content.

Keywords: PVA; Chitosan; Sulfa Drug; FTIR; Antibacterial activity

1. Introduction

Recently, polymer hydrogel can be considered as a superior material that is widely considered for diverse daily applications including medical, environmental, and industrial applications [1-6]. Both natural and synthetic polymers can be employed for synthesizing and processing polymeric hydrogels suitable for biomedical applications. Chitosan (CS) and polyvinyl alcohol (PVA) are examples of such natural and synthetic polymers that are eco-friendly and water-soluble and commonly used matrices for polymer hydrogel preparation [7,8]. Besides, their biocompatibility and hydrophilic semi-crystalline nature recommend uses in medical and environmental applications.

Chitosan is classified as a polysaccharide mainly composed of 2-amino-2-deoxy-β-D-glucopyranose synthesized via deacetylation of chitin. CS is characterized by biodegradability, biocompatibility, non-toxic, and hydrophilicity. Additionally, it displays a wide antimicrobial activity that makes them useful for tissue engineering applications [9,10].

PVA is a synthetic odorless and colorless polymer that is water-soluble used extensively in papermaking, and textile warp sizing. Besides, it was used for a variety of biomedical applications due to its biocompatibility, and the low tendency for protein adhesion [11]. PVA-based polymers are now commonly utilized in additive manufacturing. In the pharmaceutical sector, 3D printed oral dose formulations, for example, show significant promise. When PVA is used as a binder material, it is feasible to make drug-loaded tablets with changed drug-release properties [11,12]. Sulfonamides identified by Domagk were used for over 50 years as a therapeutic agent especially as antibiotic and antibacterial compartment and metabolite of red azo dye known as Prontosil [13]. Sulfonamides are also known to inhibit several enzymes such as carbonic anhydrase, cysteine protease, HIV protease, and cyclo-oxygenase [14]. Cancer chemotherapy, diuretics, and hypoglycemia are considered diseases to be treated with modified sulfonamides [15,16].

The present work is aiming to study the composite structure of **(**PVA/CS and 2-(4-hydroxyphenylhydrazono)-N-(4-sulfamoyl-phenyl)-cyanoacetamide) and their activity against different pathogenic grams for wound healing and drug delivery systems.

2. Experimental work

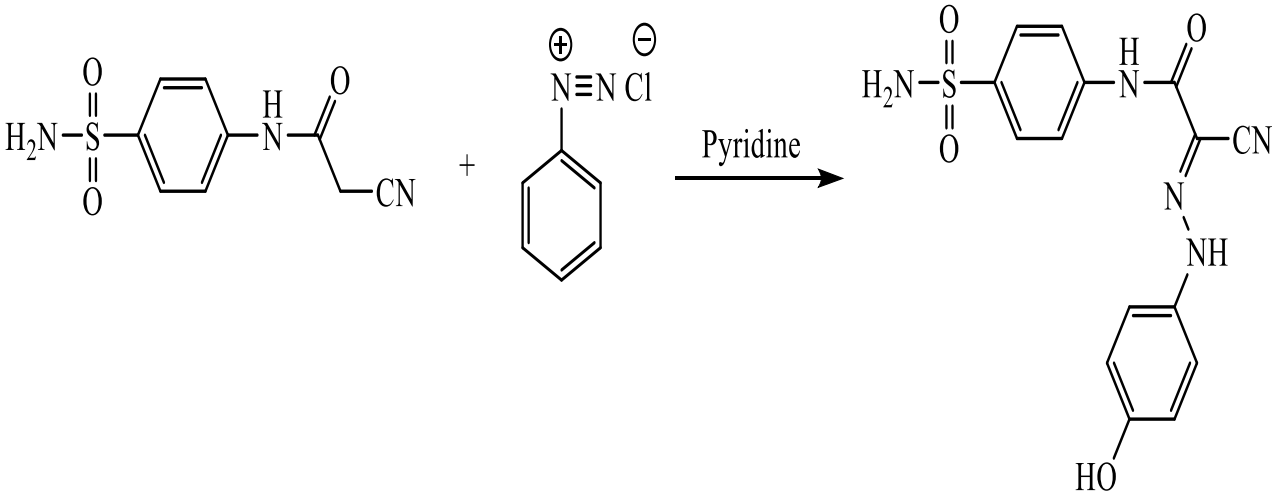
2.1. Materials

Polyvinyl alcohol (PVA) that was used for this investigation was supplied by Rasayan

Laboratory with an average molecular weight of 14,000 and high molecular weight chitosan supplied by Aldrich Co.

2.2. Preparation of 2-(4-Hydroxyphenylhydrazono)-N-(4-sulfamoylphenyl)-cyanoacetamide

A solution of sodium nitrite (0.14 g, 0.002 mol) in 3 ml water was added dropwise to a cold solution (0-5ºC) of aromatic amine (namely, 4-aminophenol, 4-aminoacetophenone and ethyl 4-aminobenzoate, 0.002 mol) in concentrated HCl (0.6 ml). The freshly prepared cold diazonium solution was added dropwise to a well-stirred cold solution (0-5°C) of cyanoacetamide derivative **33** (0.48 g, 0.002 mol) in pyridine (15 ml). The reaction mixture was stirred for 2 hours until reach a complete coupling reaction. The precipitate was filtered off, dried well, and recrystallized from ethanol/DMF mixture (3:1).



Scheme 1: Preparation of 2-(4-Hydroxyphenylhydrazono)-N-(4-sulfamoylphenyl)-cyanoacetamide

2.3. Preparation of composite films

Equal mass of both PVA and Chitosan was dissolved in distilled water and 2% aqueous solution of acetic acid respectively. After the preparation of pristine polymeric films, a mixture containing equal masses of both polymers was mixed vigorously using probe sonication for about 15 min at ambient room temperature. The solution was left for about an hour until a bubble-free solution was formed. Other samples containing the pre-calculated amount of sulfa drug were also treated by the same method. The final mixture was poured into plastic Petri dishes and kept at 50 °C for about 48 hours to remove any solvent traces. Synthesized thin films were then peeled from dishes and kept in dry until use.

2.4. Sample measurements

IR spectroscopy was used for the characterization of organic compounds through identification of the common active groups including carbonyl, amino acids, hydroxyl, etc., besides knowing of bond type. FTIR was measured using Nicolet iS10 single-beam spectrophotometer within the wavenumber range-extended between 4000-400 cm^{-1} with a resolution of about 2 cm^{-1} as an average of 32 scans. Electronic spectral data were recorded using JASCO 630 double-beam spectrometer using air as a reference material covering the range from 200 to 800 nm in absorption mode.

2.5. Antimicrobial tests

Minimum inhibition zone (MIZ) routes were employed to test the activity index of tested samples both in a pristine and composite form containing a different mass fraction of the studied drug. The experiment performed different pathogenic grams including E-coli and *Pseudomonas aeuroginosa i*s a gram-negative bacteria, *S. aureus,* and *Bacillus subtilis,* as a gram-positive bacteria, in addition to *C. Albicans* pathogenic yeast.

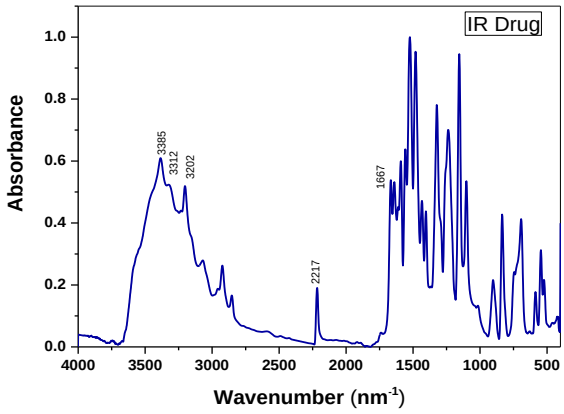
The activity index % were calculated against virgin drug using Eq. (1).

$$\text{Activity index}\,(\%) = \frac{\text{Inhibition zone of test compound (diameter) (mm)}}{\text{inhibition zone of virgin drug (mm)}} \times 100$$

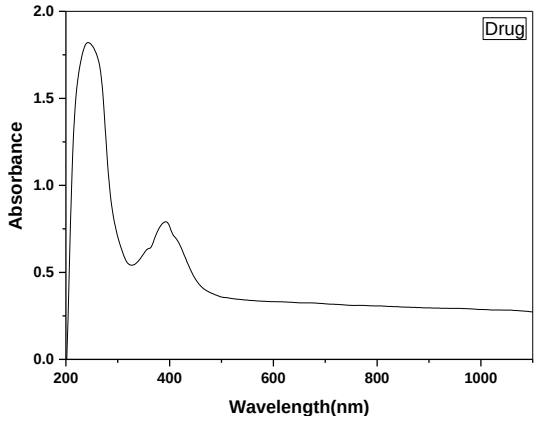
Eq. (1)

3. Results and discussion

3.1. Drug Characterization

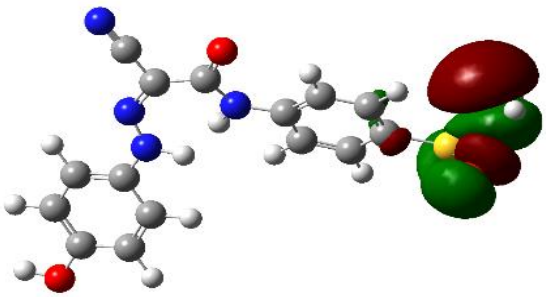


(a)

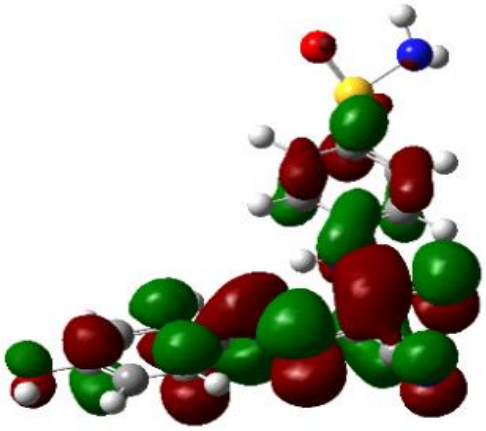


(b)

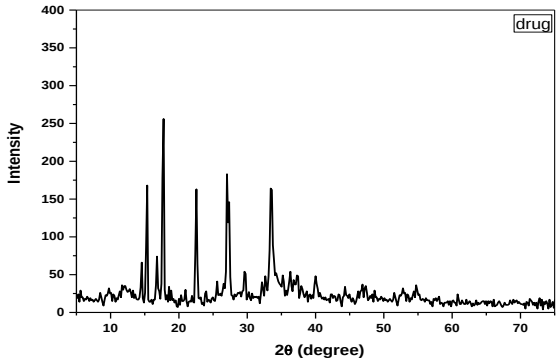
Fig. (1) reveals FTIR, UV-Visible, HUMO, LUMO and XRD analyses of the synthesized sulfa drug.



HUMO



LUMO



(c)

Fig. 1: a) FTIR, **b)** UV-Visible, **c)** HUMO & LUMO, **d)** XRD Spectra of sulfa drug

Presented data reveals that the formed drug appears as a powdered yellow-colored crystal with a melting point of about 255 °C. The reaction yield was found to be 74%. FTIR spectral data of the studied drug was characterized with bands at about 3383, 3312, 3203 related to the presence of NH_2 and OH functional groups respectively. With other two sharp bands at 2217, 1667 were usually attributed for C≡N and C=O groups in the main structure of the sulfa drug. Such observation was approved using an X-ray diffraction pattern consists of the sharp crystalline peaks in the diffractogram. UV-Vis electronic spectra show strong charge-transfer band at about 250 nm combined with a broad visible band centered at 415 nm with a shoulder at the ascending lope and without any other bands tell the end of measurements. The optical energy gap calculated from this spectrum was found to be around 5.21 eV and is in agreement with that obtained from the difference between HUMO and LOMO data.

3.2. FTIR of prepared polymeric samples

The spectral data recorded for virgin chitosan films shown in Fig. (1) reveals the appearance of characteristic bands previously reported by different authors [18]. FTIR represents an essential technique that is used in the field of polymer science by which the elaborated structural building units can be attained with spatial accuracy about published related articles. Fig. (2) reveals FT-IR spectral data of the pristine PVA and Chitosan polymer in combination with their equi-mass fraction blend prepared by solution casting route using eco-friendly solvent (Water). Fig. (3) reveals FTIR spectral absorption data of composite samples containing (PVA/CS) blends containning different mass fractions of the sulfa drug.

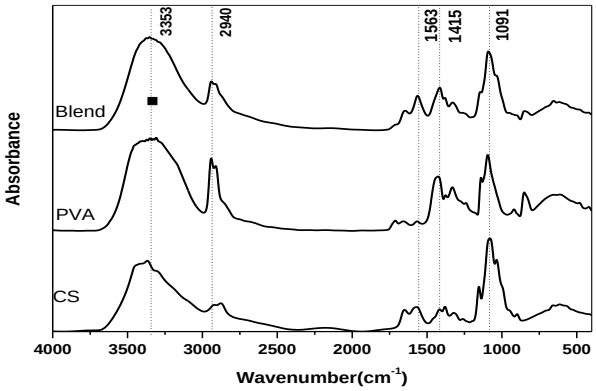


Fig. 2: FTIR absorption spectra of pristine CS, PVA, and their blend

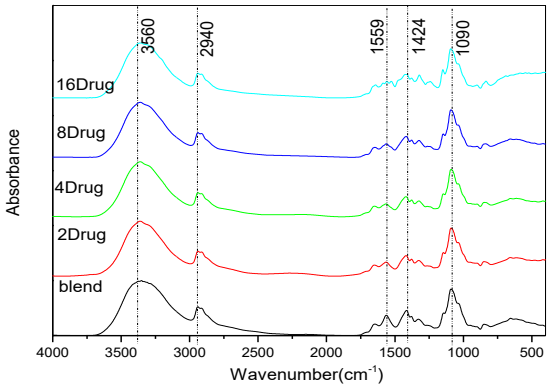


Fig. 3: FTIR of PVA\CS blend and samples contain different amount of 2-(4-hydroxy-phenylhydrazono)-N-(4-sulfamoylphenyl)-cyanoacetamide

The band originally located ~ 3350 cm^{-1} was attributed for the vibrational groups of (OH) that may be overlapped with symmetric stretching vibration of (N-H) from chitosan and hydroxyl band from the intramolecular and intermolecular hydrogen bonds of PVA. The band centered at about 2940 cm^{-1} is assigned to the carbonyl vibration of chitosan amide groups. The band at 1560 cm^{-1} was assigned to the proton amide group and determination of amide group δ (NH_3). The band located at 1415 cm^{-1} is correlated to the deformation δ(OH) while that centered at about 1370 cm^{-1} are assigned to wagging vibration of -CH_3 groups. The band originally located at 1310 cm^{-1} can be attributed for symmetric vibrations of CH_3 and in-plane vibrations of amide (-CH_2) OH deformation groups.

The band at 1150 cm^{-1} may be attributed to the asymmetric vibration of carbonyl oxygen bridges resulting from the deacetylation of chitin [19,20]. The band at 890 cm^{-1} is assigned to ω-C-H from the structure of the poly-saccharides. The band at 1750-1735 cm^{-1} may be considered to be the result of carbonyl vibration: of PVA. The band at 1140 cm^{-1} points out to the degree of sample crystallinity of sample assigned to C-O band. While the C-O-C band can be located at 1150-1085 cm^{-1} and finally the band at 1460-1470 cm^{-1} can be assigned to CH_2 vibration [21].

3.3. UV/Vis. electronic spectra of prepared polymeric samples

Fig. 4 reveals UV/visible absorption spectral data of the prepared thin films. All samples show a prominent strong charge transfer peak in the UV region at about 230 nm attributed to n→π* transition in the host polymeric matrix and point to the semi-crystalline nature of PVA.

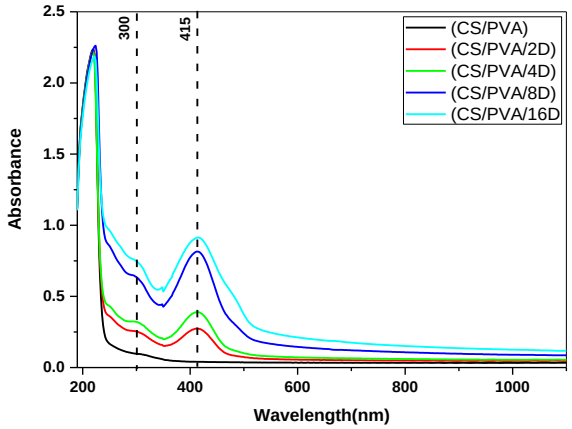


Fig. 4: UV/Vis spectroscopy of CS/PVA Blend and samples contain different amounts of 2-(4-hydroxyphenylhydrazono)-N-(4-sulfamoyl-phenyl)-cyanoacetamide

The absorption edge extended with a shoulder of increasing intensity at about 300 nm present in all curves except that of blend attributed to the interaction of the polymer with

the drug. Spectral data also shows a notable increase in the visible region band located at 415 nm with increasing drug content. Optical energy gap (E_g) both for direct and indirect transitions obtained from Tauc's plot of photon energy ($h\nu$) versus both $(\alpha h\nu)^{1/2}$ and $(\alpha h\nu)^2$, respectively were tabulated in Table (1) and shown for selected samples in Fig. (5).

Table 1: Calculated optical energy gap of studied samples

Samples	$E_{optical}$ (eV)	E_{direct}	$E_{indirect}$
CS/PVA	5.21	5.1	5.09
CS/PVA/2D	5.27	5.3	5.09
CS/PVA/4D	5.21	5.3	4.90
CS/PVA/8D	5.04	5.2	4.80
CS/PVA/16D	4.92	5.2	4.80

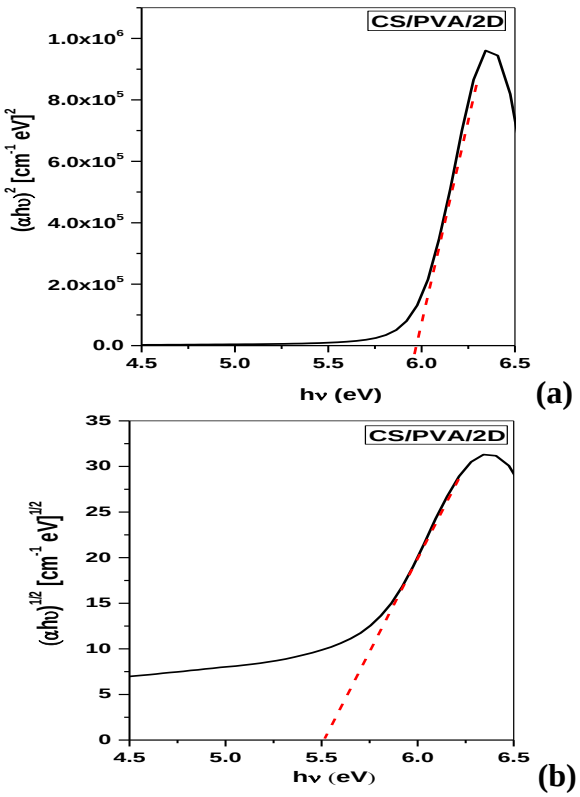


Fig. 5: Tauc's plots of sample CS/PVA/2D

3.4. Antimicrobial tests

Sulfa drugs are broadly studied and known to show wide-spectrum biocide behavior against multiple pathogenic bacteria, and yeast [22,23]. The antimicrobial activity of the synthesized sulfa drug was chosen as a reference to that of composite polymeric membranes containing a variable mass fraction of drug, All studied samples were tested against gram-negative *E. Coli* (Escherichia coli), *Pseudomonas aeuroginosa*, and gram-positive *S. aureues* (Staphylococcus aureus), and *Bacillus subtilis* pathogenic grams.

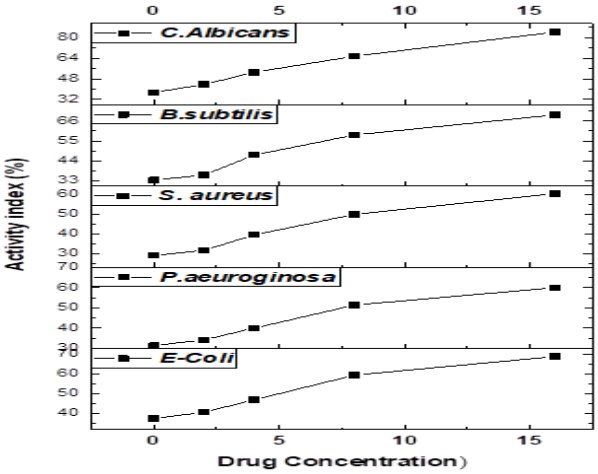


Fig. 6: Activity index versus drug concentration for the studied samples

Studied samples were also tested for their activity against pathogenic yeast *C. Albicans.* Samples were cultivated at normal body

temperature (37 °C) for 24h and the diameter of inhibition zones was then measured and recorded. Recorded inhibition zone and calculated activity were shown in Table (2) and represented in Fig. (6).

Table 2: Inhibition zone and Activity index against different pathogenic grams

Sample	*E. coli* (mg/ml)		*Pseudomonas aeuroginosa*(mg/ml)		*S. aureus* (mg/ml)		*Bacillus subtilis* (mg/ml)		*C. Albicans* (mg/ml)	
	D (mm)	A %	D (mm)	A %	D (mm)	A %	D (mm)	A %	D (mm)	A %
CS	12.0	37.50	11.0	31.43	11.0	28.95	12.0	33.33	13.0	40.63
PVA	12.0	37.50	11.0	31.43	11.0	28.95	12.0	33.33	12.0	37.50
CS/PVA/D2	13.0	40.63	12.0	34.29	12.0	31.58	13.0	36.11	14.0	43.75
CS/PVA/D4	15.0	46.88	14.0	40.00	15.0	39.47	17.0	47.22	17.0	53.13
CS/PVA/D8	19.0	59.38	18.0	51.42	19.0	50.00	21.0	58.33	21.0	65.63
CS/PVA/D16	22.0	68.75	21.0	60.00	23.0	60.53	25.0	69.44	27.0	84.38
	32.0	100	35.0	100	38.0	100	36.0	100	NA	-
	NA	-	NA	-	NA	-	NA	-	32.0	100

4. Conclusion

Thin polymeric film (PVA/Cs) containing variable content of 2-(4-Hydroxyphenyl hydrazono)-N-(4-sulfamoylphenyl)-cyanoacetamide crystal were successfully prepared using an ordinary casting route in water. Synthesized samples show no change in the optical energy gap even with a change in drug concentration. Chitosan and drug reveal chemical interaction with drugs via hydrogen bonding. All samples show wide antimicrobial behavior against studied bacteria and yeast that increases with increasing drug content.

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