Synthesis and Anti-Microbial Study of Polycyclicacetal Metal Complexes of (Hg, Ni, Co and Mn) Derived From PVA & (Formaldehyde, 4-Chlorobenzaldehyde).

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Abstract

Polymer metal complexes of poly vinyl cyclicacetal and Ni (II), Mn (II), Co (II) and Hg (II) were prepared from the reaction of PVA with formaldehyde and 4-chlorobenzaldeyde.

It has been established that, the polymer and its metal complexes showed good activities against five pathogenic bacteria (*Escherichia coli, Shigella dysentery, Klebsiella pneumonae, Staphylococcus aureus, Staphylococcus Albus*) and two fungal (*Aspergillus Niger, Yeast*) for Poly Vinyl Formal (PVF) and Poly Vinyl Benzylidene (PVB). The polymer metal complexes showed higher activity than the free polymer. The order of increasing activities was polymer < pol-Mn < pol-Ni < pol-Co □ pol-Hg for both PVF and PVB. The ability of these compounds to show antimicrobial properties suggests that, they can be further evaluated for medicinal and/or environmental applications.

Keywords: Polycyclicacetal, PVA, Polymer metal complexes, antibacterial, antifungal, activity.

Introduction

The progress made in recent years in the areas of biotechnology, tissue engineering, biomaterials, cell and molecular biology, polymer science, and other related fields has resulted in numerous medical and pharmaceutical advances. Of particular significance is the progress that has been made in the areas of implantable devices and drug/device combination products, such as drug-eluting stents [1-3], artificial organs [4-6], biosensors [7], catheters [8], scaffolds for tissue engineering, and heart valves [9,10].

Microbial infection remains one of the most serious complications in several areas, particularly in medical devices, drugs, health care and hygienic applications, water purification systems, hospital and dental surgery equipment, textiles, food packaging, and food storage. Antimicrobials gain interest from both academic research and industry due to their potential to provide quality and safety benefits to many materials. However, low molecular weight antimicrobial

agents suffer from many disadvantages, such as toxicity to the environment and short-term antimicrobial ability. To overcome problems associated with the low molecular weight antimicrobial agents, antimicrobial functional groups can be introduced into polymer molecules. The use of antimicrobial polymers offers promise for enhancing the efficacy of some existing antimicrobial agents and minimizing the environmental problems accompanying conventional antimicrobial agents by reducing the residual toxicity of the agents, increasing their efficiency and selectivity, and prolonging the lifetime of the antimicrobial agents [11].

Poly (viny1 alcohol) (PVA) is a water-soluble synthetic polymer, known to be truly biodegradable, biocompatible and of excellent film-forming properties and toughness. PVA is attracting renowned interest for the production of environmentally friendly fibers, membranes, high oxygen barrier films, etc, as well as for application in biotechnology and some medical fields [12]. Basic properties of this polymer depend strongly on the degree of polymerization, degree of hydrolysis distribution of hydroxyl groups, crystallinity, etc . PVA, like low molecular weight alcohols, is highly reactive and can undergo various modification reactions via the hydroxyl group Among them, reactions with aldehydes to form acetals such as poly(vinyl butyal) and poly(vinyl formal) are commercially utilized [13]. Many studies of the acetalization of PVA have been made since it was first investigated by Herrinann and Haehnel, the greatest part being focused on the products of high degree of acetalization [14].

Experimental

Synthesis of polycyclicacetals

Aldehyde (Formaldehyde and 4-Chloro benzaldeyde) was dissolved separately in a mixture of benzene (8ml) and ethanol (2ml) with two drops of HCl. PVA (Mw = 14000, 0.5 g) was added to the mixture with vigorous stirring at (40 – 50)°C for 24 hr. The solution was poured into excess amount of methanol (100 ml) containing equimolar amount of NaOH, the product was separated by filtration and then washed with methanol and dried under vacuum scheme (1) and (2). FTIR (KBr, cm^{-1}) for (1) & (2) is: 2953 ($C\text{-}H_{ali}$), 1238-1018 ($\text{-}C\text{-}O\text{-}C_{ace.}$), and for (2): 3057 ($C\text{-}H_{ar}$), 2991 ($C\text{-}H_{ali}$), 1279-1089 ($\text{-}C\text{-}O\text{-}C_{ace.}$)[15].

Preparation of the polycyclicacetal metal complexes

The mercury chloride ($HgCl_2$) was obtained from Fluka. Nickel chloride ($NiCl_2.6H_2O$), Manganese sulfate ($MnSO_4.H_2O$) and Cobalt chloride ($CoCl_2.H_2O$) were obtained from Aldrich. Sabouraud agar, blood agar base, MacConky agar and nutrient broth were obtained from Oxoid LTD.

The general procedure for preparation of metal complex by preparing 5% from polymer solution and mixed with equal ratios of metal solution (Co, Ni, Mn, and Hg) (10 mmol), mixture was stirred for 1 hr.

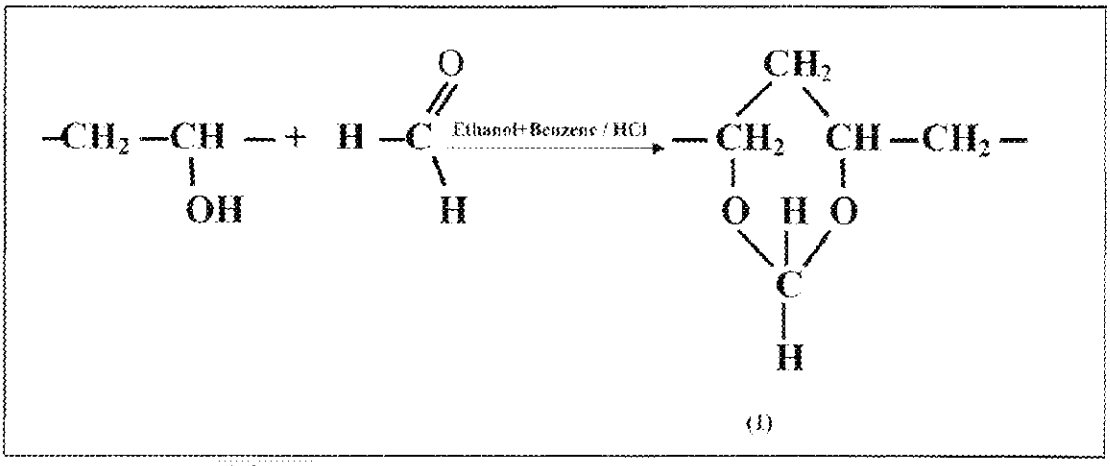
Evaluation testing of antimicrobial activity

Antimicrobial susceptibility test measures the ability of an antimicrobial agent to inhibit or kill bacterial growth In Vitro. This ability may be estimated by either the dilution method or the diffusion method. In this work we followed the broth dilution method. Certain bacteria and fungi isolates were chosen, *Escherichia-Coli*, *Shigella dysentery* and *Klebsiella Peneumoniae* were representing gm-ve isolates, *Staphylococcus aureus* and *Staphylococcus albeus* were representing gm+ve isolates, two fungal (*Aspergillus niger, Yeast*). Those Isolates were taken from about 50 patients at CPHL (Central Public Health Laboratory in Baghdad).

The broth dilution method: Serial twofold dilutions of an antimicrobial agent are incorporated into broth containing tubes that are then inoculated with a standard number of organisms usually 10^5-10^6 Colony-Forming Units (CFU) per milliliter. After the culture has been incubated at $37C^0$ for 18 hr. The lowest concentration that prevents growth after overnight incubation is known as the Minimum Inhibitory Concentration (MIC) of the agent, The MIC is defined as the lowest concentration of antimicrobial agent at which there is no visible growth [16-17].

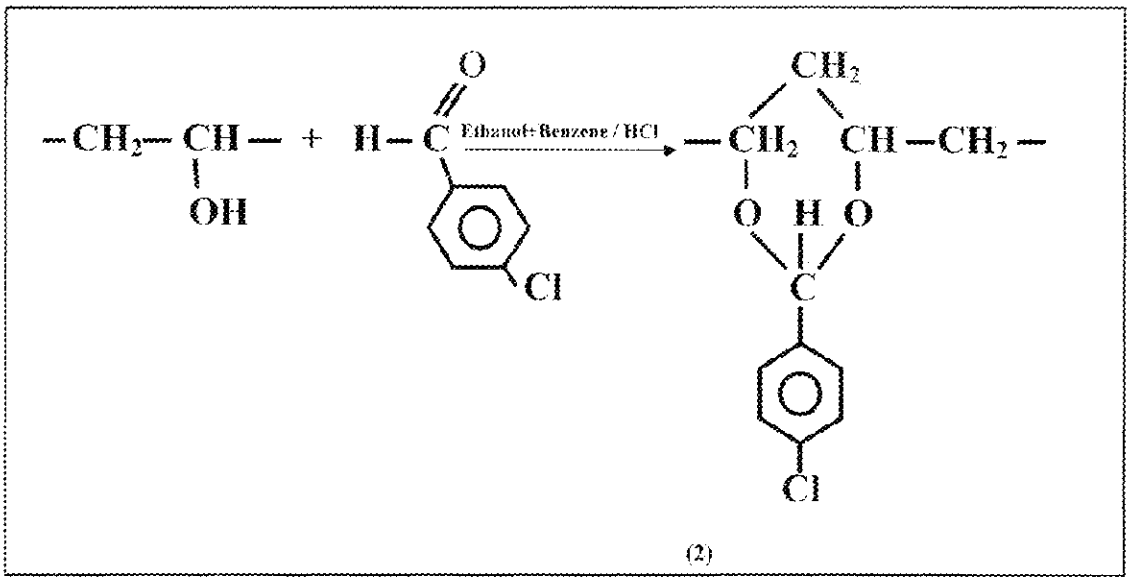
Results and Discussion

Compounds (1, 2) were prepared from treatment of polyvinyl alcohol with formaldehyde and 4-Chloro benzaldehyde respectively, in presence of hydrochloric acid with ethanol and benzene as solvents with stirring for 24 hours (scheme 1, 2), which were converted to PVAcyclicacetal. The FTIR spectrum for compounds (1, 2) confirm the formation of the polycyclicacetal by disappearance of the band (1749) cm^{-1} and (1731) cm^{-1} for ($C=O_{ald.}$) for compound (1) and (2) respectively and the appearance of the band 1238-1018 (-C-O-$C_{ace.}$)and (1279-1089) cm^{-1} for (-C-O-$C_{ace.}$) for compound (1)and (2) respectively.



(1)

Scheme (1): The scheme of prepared poly vinyl formal (PVF).



(2)

Scheme (2): The scheme of prepared poly vinyl benzylidene (PVBenz).

Antimicrobial studies

Antibacterial activity of the synthesized compounds and their corresponding metal complexes was determined against three Gram-negative bacterial strains (*Escherichia coli*, *Shigella dysentery* and Klebsiella *Pneumoniae*), two Gram–positive bacterial strains (*Staphylococcus aureus* and *Staphylococcus Albus*) and two fungal (*Aspergillus niger* and *Yeast*) Tables (1-10) for PVF and (11-20) for PVB respectively.

Table (1) Effect of (PVF) on the growth of selected bacteria isolated.

Isolates	Gram Stain	Concentration µg/ml											
		700	750	800	850	900	950	1000	1050	1100	1150	1200	1250
Escherichia coli	-ve	+	+	+	+	+	+	+	+	-	-	-	-
Shigella dysentery	-ve	+	+	+	+	+	+	+	+	+	-	-	-
Klebsiella pneumoniae	-ve	+	+	+	+	+	+	+	+	+	+	-	-
Staphylococcus aureus	+ve	+	+	+	+	+	+	+	+	+	+	+	-
Staphylococcus albus	+ve	+	+	+	+	+	+	+	+	+	+	+	-

Table (2) Effect of (PVF-Hg) on the growth of selected bacteria isolated.

Isolates	Gram Stain	Concentration µg/ml											
		10	20	30	40	50	100	150	200	250	300	350	400
Escherichia coli	-ve	+	+	-	-	-	-	-	-	-	-	-	-
Shigella dysentery	-ve	+	+	+	-	-	-	-	-	-	-	-	-
Klebsiella pneumoniae	-ve	+	+	-	-	-	-	-	-	-	-	-	-
Staphylococcus aureus	+ve	+	+	+	-	-	-	-	-	-	-	-	-
Staphylococcus albus	+ve	+	+	+	-	-	-	-	-	-	-	-	-

Table (3) Effect of (PVF-Co) on the growth of selected bacteria isolated.

Isolates	Gram Stain	Concentration µg/ml											
		450	500	550	600	650	700	750	800	850	900	950	1000
Escherichia coli	-ve	+	+	+	+	+	+	+	+	+	-	-	-
Shigella dysentery	-ve	+	+	+	+	+	+	+	+	-	-	-	-
Klebsiella pneumoniae	-ve	+	+	+	+	+	+	+	+	+	+	-	-
Staphylococcus aureus	+ve	+	+	+	+	+	+	+	+	-	-	-	-
Staphylococcus albus	+ve	+	+	+	+	+	+	+	+	+	-	-	-

Table (4) Effect of (PVF -Ni) on the growth of selected bacteria isolated.

Isolates	Gram Stain	Concentration µg/ml											
		450	500	550	600	650	700	750	800	850	900	950	1000
Escherichia coli	-ve	+	+	+	+	+	+	+	-	-	-	-	-
Shigella dysentery	-ve	+	+	+	+	+	+	+	+	+	-	-	-
Klebsiella pneumoniae	-ve	+	+	+	+	+	+	+	+	-	-	-	-
Staphylococcus aureus	+ve	+	+	+	+	+	+	+	+	+	-	-	-
Staphylococcus albus	+ve	+	+	+	+	+	+	+	+	-	-	-	-

Table (5) Effect of (PVF-Mn) on the growth of selected bacteria isolated.

Isolates	Gram Stain	Concentration µg/ml											
		450	500	550	600	650	700	750	800	850	900	950	1000
Escherichia coli	-ve	+	+	+	+	+	+	+	+	+	+	-	-
Shigella dysentery	-ve	+	+	+	+	+	+	+	+	+	-	-	-
Klebsiella pneumoniae	-ve	+	+	+	+	+	+	+	+	+	-	-	-
Staphylococcus aureus	+ve	+	+	+	+	+	+	+	+	+	+	+	-
Staphylococcus albus	+ve	+	+	+	+	+	+	+	+	+	+	+	-

Table (6) Effect of (PVF) on the growth of selected fungi isolated.

Isolates	Concentration µg/ml										
	1000	1050	1100	1150	1200	1250	1300	1350	1400	1450	1500
Aspergillus niger	+	+	+	+	+	+	+	+	+	-	-
Yeast	+	+	+	+	+	+	+	+	+	-	-

Table (7) Effect of (PVF-Hg) on the growth of selected fungi isolated.

Isolates	Concentration µg/ml										
	750	800	850	900	950	1000	1050	1100	1150	1200	1250
Aspergillus niger	+	+	+	-	-	-	-	-	-	-	-
Yeast	+	+	+	+	+	-	-	-	-	-	-

Table (8) Effect of (PVF-Co) on the growth of selected fungi isolated.

Isolates	Concentration µg/ml										
	850	900	950	1000	1050	1100	1150	1200	1250	1300	1350
Aspergillus niger	+	+	+	+	+	+	+	-	-	-	-
Yeast	+	+	+	+	+	+	+	+	-	-	-

Table (9) Effect of (PVF-Ni) on the growth of selected fungi isolated.

Isolates	Concentration µg/ml										
	850	900	950	1000	1050	1100	1150	1200	1250	1300	1350
Aspergillus niger	+	+	+	+	+	+	+	+	-	-	-
Yeast	+	+	+	+	+	+	+	-	-	-	-

Table (10) Effect of (PVF-Mn) on the growth of selected fungi isolated.

Isolates	Concentration µg/ml										
	1000	1050	1100	1150	1200	1250	1300	1350	1400	1450	1500
Aspergillus niger	+	+	+	+	+	+	+	+	-	-	-
Yeast	+	+	+	+	+	+	+	-	-	-	-

Table (11) Effect of (PVB) on the growth of selected bacteria isolated.

Isolates	Gram Stain	Concentration µg/ml											
		550	600	650	700	750	800	850	900	950	1000	1050	1100
Escherichia coli	-ve	+	+	+	+	+	+	+	-	-	-	-	-
Shigella dysentery	-ve	+	+	+	+	+	+	+	-	-	-	-	-
Klebsiella pneumoniae	-ve	+	+	+	+	+	+	+	+	-	-	-	-
Staphylococcus aureus	+ve	+	+	+	+	+	+	+	-	-	-	-	-
Staphylococcus albus	+ve	+	+	+	+	+	+	+	+	-	-	-	-

Table (12) Effect of (PVB-Hg) on the growth of selected bacteria isolated.

Isolates	Gram Stain	Concentration µg/ml											
		10	20	30	40	50	100	150	200	250	300	350	400
Escherichia coli	-ve	+	-	-	-	-	-	-	-	-	-	-	-
Shigella dysentery	-ve	+	-	-	-	-	-	-	-	-	-	-	-
Klebsiella pneumoniae	-ve	+	-	-	-	-	-	-	-	-	-	-	-
Staphylococcus aureus	+ve	+	+	-	-	-	-	-	-	-	-	-	-
Staphylococcus albus	+ve	+	+	-	-	-	-	-	-	-	-	-	-

Table (13) Effect of (PVB-Co) on the growth of selected bacteria isolated.

Isolates	Gram Stain	Concentration µg/ml											
		450	500	550	600	650	700	750	800	850	900	950	1000
Escherichia coli	-ve	+	+	+	+	+	-	-	-	-	-	-	-
Shigella dysentery	-ve	+	+	+	+	-	-	-	-	-	-	-	-
Klebsiella pneumoniae	-ve	+	+	+	+	+	+	+	-	-	-	-	-
Staphylococcus aureus	+ve	+	+	+	+	+	+	-	-	-	-	-	-
Staphylococcus albus	+ve	+	+	+	+	+	+	-	-	-	-	-	-

Table (14) Effect of (PVB-Ni) on the growth of selected bacteria isolated.

Isolates	Gram Stain	Concentration µg/ml											
		450	500	550	600	650	700	750	800	850	900	950	1000
Escherichia coli	-ve	+	+	+	+	+	+	-	-	-	-	-	-
Shigella dysentery	-ve	+	+	+	+	+	+	-	-	-	-	-	-
Klebsiella pneumoniae	-ve	+	+	+	+	+	+	-	-	-	-	-	-
Staphylococcus aureus	+ve	+	+	+	+	+	+	-	-	-	-	-	-
Staphylococcus albus	+ve	+	+	+	+	+	+	+	-	-	-	-	-

Table (15) Effect of (PVB-Mn) on the growth of selected bacteria isolated.

Isolates	Gram Stain	Concentration µg/ml											
		450	500	550	600	650	700	750	800	850	900	950	1000
Escherichia coli	-ve	+	+	+	+	+	+	+	+	-	-	-	-
Shigella dysentery	-ve	+	+	+	+	+	+	+	-	-	-	-	-
Klebsiella pneumoniae	-ve	+	+	+	+	+	+	+	-	-	-	-	-
Staphylococcus aureus	+ve	+	+	+	+	+	+	+	+	-	-	-	-
Staphylococcus albus	+ve	+	+	+	+	+	+	+	+	+	-	-	-

Table (16) Effect of (PVB) on the growth of selected fungi isolated.

Isolates	Concentration µg/ml										
	1000	1050	1100	1150	1200	1250	1300	1350	1400	1450	1500
Aspergillus niger	+	+	+	+	+	+	-	-	-	-	-
Yeast	+	+	+	+	+	+	+	-	-	-	-

Table (17) Effect of (PVB-Hg) on the growth of selected fungi isolated.

Isolates	Concentration µg/ml										
	750	800	850	900	950	1000	1050	1100	1150	1200	1250
Aspergillus niger	+	-	-	-	-	-	-	-	-	-	-
Yeast	+	+	+	-	-	-	-	-	-	-	-

Table (18) Effect of (PVB-Co) on the growth of selected fungi isolated.

Isolates	Concentration µg/ml										
	850	900	950	1000	1050	1100	1150	1200	1250	1300	1350
Aspergillus niger	+	+	+	+	-	-	-	-	-	-	-
Yeast	+	+	+	+	+	-	-	-	-	-	-

Table (19) Effect of (PVB-Ni) on the growth of selected fungi isolated.

Isolates	Concentration µg/ml										
	850	900	950	1000	1050	1100	1150	1200	1250	1300	1350
Aspergillus niger	+	+	+	+	+	+	+		-	-	-
Yeast	+	+	+	+	+	-	-	-	-	-	-

Table (20) Effect of (PVB-Mn) on the growth of selected fungi isolated.

Isolates	Concentration µg/ml										
	1000	1050	1100	1150	1200	1250	1300	1350	1400	1450	1500
Aspergillus niger	+	+	+	+	+	-	-	-	-	-	-
Yeast	+	+	+	+	+	+	+	-	-	-	-

The synthesized polycyclicacetal and all polymer complexes exhibited a good degree of inhibitory effects on the growth of different bacteria and fungi isolates. Antimicrobial agents may affect cells in a variety of ways, many of which are poorly understood [18], most of the commonly used antibacterial chemotherapeutic agents act by one of the following basic mechanisms: competitive antagonism of some metabolite, inhibition of bacterial cell wall synthesis, action on cell membranes, inhibition of protein synthesis, or inhibition of nucleic acid synthesis [19].

The results indicate that the polymer metal complexes show more activity than the free polymer under similar experimental conditions. This would suggest that the chelation could facilitate the ability of a complex to cross a cell membrane as explained by Tweedy's chelation theory (Cotton and Wilkinson, 1972) [20]. Chelation considerably reduces the polarity of the metal ion mainly because of partial sharing of its positive charge with the donor groups and possible electron delocalization over the whole chelate ring. Such chelation could also enhance the lipophilic character of the central metal atom, which subsequently favors its permeation through the lipid layer of the cell membrane [21, 22].

The Compounds (PVF-Hg) and (PVB-Hg) were, however, found to be active against all the bacteria and fungi. To the contrary, the compoundS (PVF), (PVB), (PVF-Co), (PVF-Ni), (PVF-Mn), (PVB-Co), (PVB-Ni) and (PVB-Mn) were found to be low active against the all bacteria and fungi.

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تحضير معقدات بوليمر الاسيتال الحلقي المعدني لكل من (الزئبق والنيكل والكوبلت والمنغنيز) والمشتقة من تفاعل بوليمر الفنيل الكحولي مع كل من الفورمالديهايد و 4-كلورو بنزالديهايد، مع دراسة فعاليتها المضادة للمايكروبات

طه مهدي صالح

قسم العلوم / كلية التربية الاساسية / الجامعة المستنصرية

الخلاصة:

تم تحضير معقدات البوليمر المعدنية من بوليمر الفتيل الكحولي والمعادن مثل (النيكل والمنغنيز والكوبلت والزئبق) وذلك بتفاعل البوليمر الفنيل الكحولي مع كل من الفورمالديهايد وال 4-كلوروبنزالديهايد.

أظهرت النتائج بأن معقدات البوليمر المعدنية لكل من البولي فتيل الفورمالي والبولي فنيل البنزلديهايدي قد اعطت فعالية جيدة لخمس انواع من البكتريا المسببة للامراض وهي (*Escherichia coli, Shigella dysentery, Klebsiella pneumonae, Staphylococcus aureus, Staphylococcus Albus*) وإثنان من الطحالب وهي (*Aspergillus Niger, Yeast*). حيث أظهرت معقدات البوليمر المعدنية اكثر فاعلية من البوليمر لوحده وكان ترتيب الفعالية ولكلا البوليمر الفنيل الفورمالي والبنزالديهايدي كما يلي{البوليمر < نوليمر-منغنيز < بوليمر- نيكل < بوليمر – كوبلت < بوليمر – زئبق}.

وبذلك فان فاعلية هذه المواد تكون مرشحة لاستخدامها في المجالات الطبية أو في التطبيقات البيئية.

مفتاح الكلمات: بوليمر الاسيتال الحلقي، PVA، معقدات البوليمر المعدني، فعالية مضادة للمايكروبات، فعالية مضادة للطحالب.