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Synthesize and Characterization of New Polydimethylsiloxane Derivatives with Evaluation of Biological Activities

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ABSTRACT

New polymers of silicone derivatives were prepared. The polymers were characterized by IR, NMR spectrophotometry. The biological activity against Streptococcus, E-Coli, Pseudomonas, Staphylococcus, Klebsiella were studied. The new polymers have shown more activity against Pseudomonas, Staphylococcus aureus, Klebsiella. The wound dressing studied on New Zealand White Rabbits (5 groups) each group contained 6 rabbits (3 male and 3 female), each animal had made 2 wounds,one for control (povidone-iodine, silicone gel) and other for our compounds, all products showed good activity on open wounds more than drugs in market. Benzaldehyde is consists of benzene bearing a single formyl substituent; the simplest aromatic aldehyde and parent of the class of benzaldehydes. It has a role as a flavoring agent, a fragrance, an odorant receptor agonist. Polyvinylpyrrolidone has disinfectant properties, so we used it in our compound to become more potent.

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INTRODUCTION

Multiple biological, non-natural, and hybrid polymers are used for multiple medical applications. A wide range of different polymers is existing, and they have further the benefit to be tunable in physical, chemical, and biological properties in a varied range to match the desires of specific applications (Thomas, 2000)

Synthetic polymers gained high attractiveness for technical as well as for medical applications for various reasons. A wide range of physical and chemical properties can be accomplished based on the monomer units, polymerization reaction, and formation of copolymers containing different components at regulating concentrations (Maitz, 2015).

One of the most significant synthetic polymers is silicone.

Silicones consist of an –Si–O– backbone with different chain lengths and crosslinks, which conclude mechanical properties from liquid oil via a gel construction to rubber elastomer. The side chains may be improved, but in the most communal poly(dimethylsiloxane) (PDMS), they are methyl groups. (Wacker, 2014)

Polydimethylsiloxane (PDMS) is the best-known organosilicon rubbery polymer.

Thermal stability, Good resistance to UV radiation. Exceptional release properties and surface activity. High permeability to gases. Good damping activities, antifriction, and lubricity. Hydrophobic and physiological inertness.

High inertness in physiological surroundings makes it likely to use this material in altered biomedical uses, including soft matrix for drug delivery, cosmetics, wound dressing. (Gardner *et al.*, 2001)

Benzaldehyde is involved benzene bearing a single formyl substituent, the simplest aromatic aldehyde and parent of the class of benzaldehydes. It has a role as a flavoring agent, a fragrance, an odorant receptor agonist. Benzaldehyde seems like a clear colorless to yellow liquid; it odors a little like almond and has a hot, aromatic taste. Benzaldehyde is very soluble in water. Benzaldehyde happens naturally in plants. It can be produced in the atmosphere from the reaction of certain chemicals with sunlight.

It is used as a preservative in cosmetics, personal care products, as a solvent for oils, flavoring, and unnatural perfumes. It may be a tobacco additive. It was previously used as an insecticide. Because Benzaldehyde quickly metabolizes to Benzoic Acid in the skin, the obtainable dermal irritation and sensitization data demonstrating no undesirable reactions to Benzoic Acid were regard as supportive of the safety of Benzaldehyde. Benzaldehyde is absorbed within the skin and by the lungs, allocates to all well-perfused organs, but does not store in any specific tissue type. (Göthlich *et al.*, 2005).

Polyvinylpyrrolidone (PVP), also generally called polyvidone or povidone, is a water-soluble polymer prepared from the monomer -vinylpyrrolidone. *(Haaf et al., 1985)*

PVP added to iodine forms a complex called povidone-iodine that possesses disinfectant properties. This complex is used in different products, similar solutions, ointment, pessaries, liquid soaps, and surgical scrubs. (Bühler and Volker, 2005).

MATERIALS AND METHODS

Chemicals

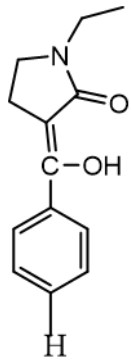
The chemical compounds and agars used in an experimental will be mentioned in Table 1.

Synthesis of the compounds

The new products are prepared by the following methods, as shown in Table 2

Preparation of Polyvinyl pyrrolidone _ Benzyldehyde PVB

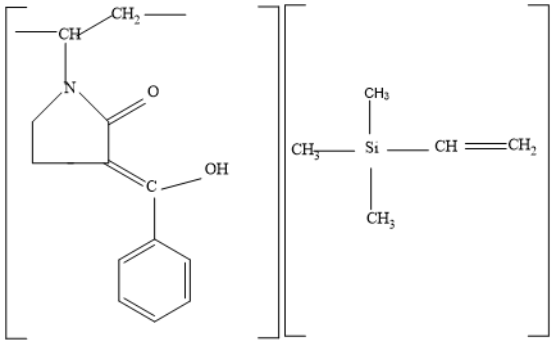
Dissolve 10 moles (1.1g) of PVP in 10 ml ethanol in 60c ° with stirring then add 5ml of alcoholic KOH; the colour became yellow, last added 10mmole of B. D (1g) immediately the colour change to obtain on the yellow liquid product and reflux for 2hrs with stirring. Neutralized the solution with 10% HCL till the PH became 7, filtered the product to remove the precipitate, and evaporate the solvent in 70c° for about 3 hr to give the viscous oily yellowish product. As shown in Scheme 1. (Wilson and Gisvold, 2004).



Scheme 1: PVB

Preparation of polyvinyl pyrrolidone _Benzaldeh_VinylTrimethylSilane VS.PVB

TMS vinyl terminated 5.3 ml (25 mmoles) added to 100mmole (22g)of PVB that prepared in step 3 in sealed round bottom flask (25ml)and reflux about $\frac{1}{2}$ hrs in 70 c° then evaporate the solvent on 50c° for about 1 hr to obtained on pale yellow gel product. As shown in Scheme 2.



Scheme 2: VS.PVB

Preparation of Polyvinyl pyrrolidone _Paraflurobenzyldehyde F.PVB

Take 10 mmoles (1.1g) of PVP in 10ml ethanol in 60c° with steering then add 5ml of alcoholic KOH the colour became yellow, last added 10mmole of para fluoro B.D (1.24g) immediately the color change to obtained on yellow liquid product and reflux for 2hrs with steering. Neutralized the solution with 10% HCL till the PH became 7, filtered the product to remove the precipitate, and evaporate the solvent

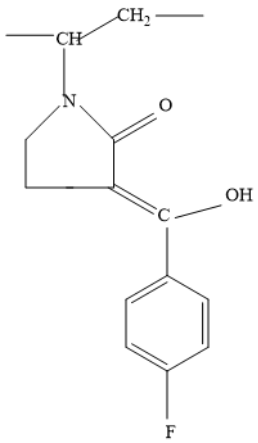
Table 1: Chemicals, Agars, and their suppliers

No	Chemicals and Agars	Origin
1	Vinyltrimethylsilane VTMS	Sigma Aldrich - Germany
2	Absolute ethanol	Sigma Aldrich - Germany
3	Polyvinylpyrrolidone PVP	Sigma Aldrich - Germany
4	Benzaldehyde BD	Sigma Aldrich - Germany
5	Parafluro benzaldehyde para F.BD	Merk - Germany
6	Parahydroxy benzaldehyde para OH.BD	ALPHA - India
7	para methoxy benzaldehyde para OCH3.BD	Merk - Germany
8	Potassium hydroxide KOH	Schariab - Spain
9	Nutrient agar	OXOID - England
10	Nutrient broth	OXOID – England
11	Silicone gel	Philadelphia – Jordan
12	Povidone-iodine	Jou pharm. - Egypt

Table 2: The synthesized compounds

NO	Name of compounds	Symbol
1	Polyvinyl pyrrolidone _ Benzyldehyde	PVB
2	polyvinyl pyrrolidon_Benzaldehyde_VinylTrimethylSilane	VS.PVB
3	Polyvinyl pyrrolidone _Paraflurobenzyldehyde	F.PVB
4	Polyvinyl pyrrolidone _Paraomethoxyobenzyldehyde	OCH3.PVB
5	Polyvinyl pyrrolidone _Parahydroxybenzyldehyde	OH.PVB

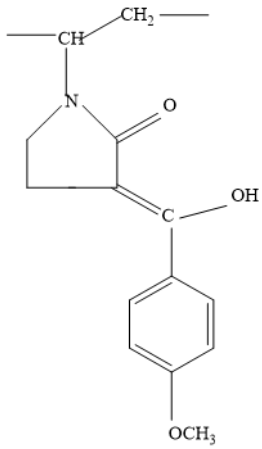
in 70c° for about 3hr to give a yellowish viscous oily product. As shown in Scheme 3



Scheme 3: F.PVB

Preparation of Polyvinyl pyrrolidone _Paraomethoxyobenzyldehyde OCH_3.PVB

Ten mmoles (1.1g) of PVP dissolved in 10ml ethanol in 60c ° with steering then add 5ml of alcoholic KOH the colour became yellow, last added 10mmole of para methoxy B. D (1.36g) immediately the colour change to obtained on yellow liquid product and reflux for 2hrs with steering. Neutralized the solution with 10% HCL till the PH became 7, filtered the product to remove the precipitate, and evaporate the solvent in 70c° for about 3 hr. To give a viscous oily brownish product. As shown in Scheme 4.

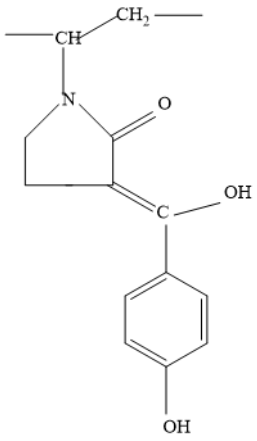


Scheme 4: OCH_3.PVB

Preparation of Polyvinyl pyrrolidone _Parahydroxybenzyldehyde OH.PVB

Five mmoles (0.65g) of PVP melt in 5ml ethanol in 60c ° with steering then add 3ml of alcoholic KOH the colour became yellow, last added 5mmole of para hydroxy B. D (6.1g) immediately the colour change to obtained on the pink liquid product and

reflux for 2hrs with steering. Neutralized the solution with 10% HCL till the PH became 7, filtered the product to remove the precipitate, and evaporate the solvent in 70c° for about 3 hr. To give a viscous oily orange products. As shown in Scheme 5.



Scheme 5: OH.PVB

Analytical Techniques

FT.IR Spectra

FT.IR spectra for all studied compounds were calculated as KBr disks using FT.IR 8400S SHIMADZU (Japan), in the technique Laboratory of Pharmaceutical Chemistry Department / College of Pharmacy / Basrah University. (Smith and W., 1976)

^{1} H-NMR Spectra

The studied compounds were achieved at the analytical Laboratory of Tehran University/College of sciences /Chemistry department, using 500MHz NMR (INOVA Switzerland). DMSO-d_6 was used as a solvent and TMS as an internal standard. (Shah *et al.*, 2006)

RESULTS AND DISCUSSION

The involved study synthesis of the new compound from polyvinylpyrrolidone and benzaldehyde which followed by prepared new compound of polydimethylsiloxane derivatives which predicted by the following,

FT-IR Spectrum of PVB

The compound PVB show strong absorption band at 3452 cm^{-1} refer to O-H stretching, the medium band 2881-2951 cm^{-1} attributed C-H stretching of aliphatic alkyl, medium band at 1427cm^{-1} refer to C-H bending, strong band at 1670 cm^{-1} attributed to N-C=O stretching, 1168cm^{-1} medium band attributed C-N stretching, at 1496cm^{-1}refer to C=C aromatic, medium band at 1604 cm^{-1} refer to C=C stretching (-C=C-OH)

FT-IR Spectrum of F.PVB

The more characteristic band in IR spectrum of F.PVB Figure 1 compound is C-F show medium absorption band at 1041cm^{-1}stretching, strong band at 3448 cm^{-1} refer to O-H stretching, the medium band 2881-2951 cm^{-1} attributed C-H stretching of aliphatic alkyl, medium band at 1427 cm^{-1} refer to C-H bending , strong band at 1678 cm^{-1} attributed to N-C=O stretching, 1161cm^{-1} medium band attributed C-N stretching, medium band at 1600 cm^{-1} refer to C=C stretching (-C=C-OH), medium band 1508cm^{-1}attributed to C=C aromatic at 1041cm^{-1} medium band related to C-F stretching.

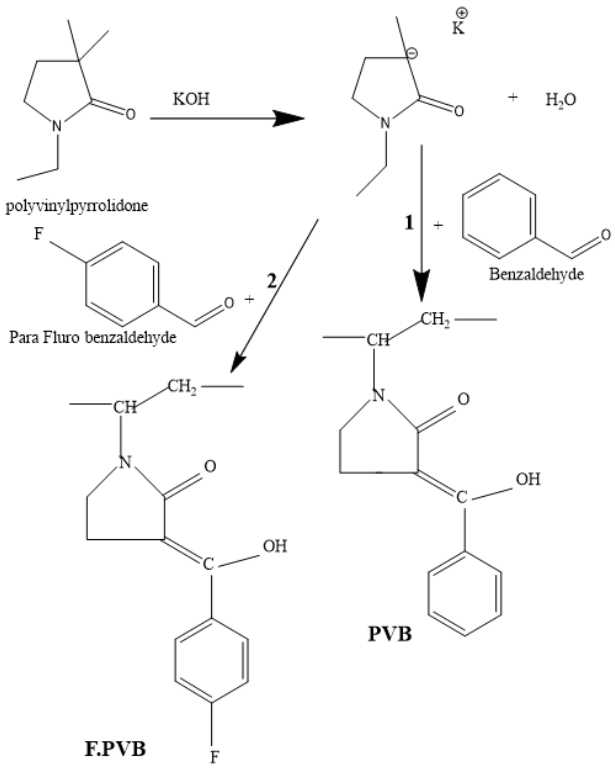


Figure 1: F.PVB

FT-IR Spectrum of OH.PVB

The IR spectrum of OH.PVB compound show weak absorption band at 3498cm^{-1} refer to O-H stretching, the weak band 2823-2955 cm^{-1} attributed C-H stretching of aliphatic alkyl, medium band at 1438 cm^{-1} refer to C-H bending, strong band at 1674 cm^{-1} attributed to N-C=O stretching, 1288cm^{-1} medium band attributed C-N stretching, medium band at 1581 cm^{-1} refer to C=C stretching (-C=C-OH), medium band 1500cm^{-1}attributed to C=C aromatic at 1149cm^{-1} medium band related to C-O stretching.

FT-IR Spectrum of OCH_3 PVB

The compound OCH_3PVB show weak absorption

Table 3: Inhibition zone of tested compounds and standard drugs

S.aureus compounds	P.aeruginosa	E.coli	Klebsiella	Conc. (μg/ml)	
0	5	0	0	100	PVB
3	6	0	0	250	
3	7	6	0	500	
3	7	0	0	750	
5	8	7	0	1000	
10	10	10	14	5000	
0	0	0	0	100	F.PVB
0	3	0	0	250	
3	0	0	0	500	
3	0	0	0	750	
3	0	10	0	1000	
7	9	8	15	5000	
3	3	0	0	100	OH.PVB
3	4	3	0	250	
3	4	4	0	500	
4	4	4	0	750	
0	4	4	0	1000	
0	4	4	0	5000	
3	4	0	0	100	OCH_3PVB
3	5	0	0	250	
3	5	0	0	500	
3	5	3	0	750	
3	5	7	0	1000	
8	8	8	9	5000	
0	0	0	0	100	VS.PVB
3	0	0	0	250	
3	0	0	0	500	
3	0	0	0	750	
3	0	0	0	1000	
8	8	13	14	5000	

Table 4: Groups of animals treated with products

No. of group	Product at site A	Control at site B
Group 1	PVB	Povidone-iodine
Group 2	F.PVB	Povidone-iodine
Group 3	OCH_3PVB	Povidone-iodine
Group 4	OH.PVB	Povidone-iodine
Group 5	VS.PVB	Silicone gel

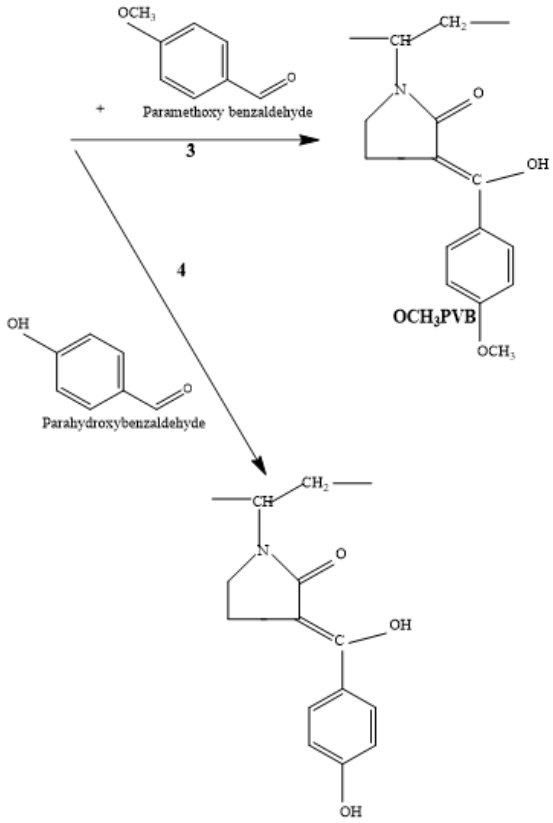


Figure 2: OCH_3 PVB

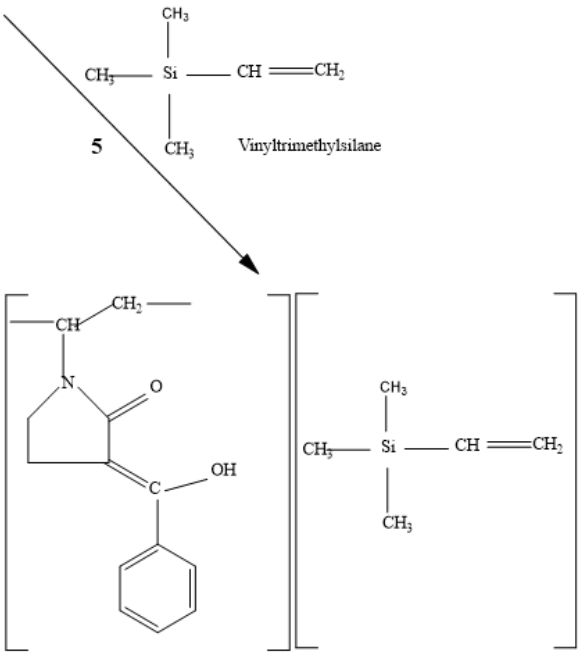


Figure 3: VS.PVB

band at 3479 cm^{-1} refer to O-H stretching , the medium band 2843-2951 cm^{-1} attributed C-H stretching of aliphatic alkyl, medium band at 1427cm^{-1} refer to C-H bending, strong band at 1678 cm^{-1} attributed to N-C=O stretching, 1161cm^{-1} medium band attributed C-N stretching, at 1512cm^{-1}refer to C=C aromatic, medium band at 1600 cm^{-1} refer to C=C stretching (-C=C-OH), medium band at 1022cm^{-1} related to C-O in (C-OCH_3) Figure 2

FT- IR Spectrum of VS.PVB

The medium absorption band at 3448 cm^{-1} showed in the IR spectrum of VS. PVB compound refer to O-H stretching, the medium band 2881-2955 cm^{-1} attributed C-H stretching of aliphatic alkyl, medium band at 1458 cm^{-1} refer to C-H bending, strong band at 1670 cm^{-1} attributed to N-C=O stretching, medium band at 1597 cm^{-1} refer to C=C stretching, medium band at 1168cm^{-1} refer to C-N stretching, strong band at 1693cm^{-1} refer to C=C of VTMS polymer stretching, medium band at 1145cm^{-1} attributed to Si-$(CH_3)_3$ stretching. Figure 3

^{1} H-NMR Spectrum PVB

The ^{1}H-NMR spectrum of compound PVB displayed characteristic aliphatic signals of alkyl chain protons represented by the following, triplet signal at 1.0 ppm related to protons of -CH_2- group, 3.4 ppm patent related to -CH- (-CH-CH_2-), another signal at 7.5-8.0 ppm related to aromatic ring, at 10.0 ppm related to OH group, as shown as in Scheme 1

^{1} H-NMR Spectrum F.PVB

The ^{1}H-NMR spectrum of compound F.PVB exhibited specific aliphatic signals of alkyl chain protons signified by the following, triplet signal at 1.0 ppm related to protons of -CH_2- group, 3.4 ppm patent related to -CH- (-CH-CH_2-), another signal at 7.5-8.0 ppm related to aromatic ring, at 10.0,9.9 ppm two singular signal related to OH group due to geometric isomer (cis and trans), as shown as in Scheme 3

^{1} H-NMR Spectrum OCH_3PVB

The compound OCH_3.PVB presented triplet signal at 1.0 ppm linked to protons of -CH_2- group, 3.4 ppm patent related to -CH- (-CH-CH_2-), another signal at 7.5-8.0 ppm related to aromatic ring , at 10.0 ppm correlated to OH group, singular signal shown at 3.8ppm related to CH_3 (OCH_3) as shown as in Scheme 4

^{1} H-NMR Spectrum OH.PVB

The ^{1}H-NMR spectrum of compound 0H.PVB showed triplet signal at 1.0 ppm referred to protons of -CH_2- group, 3.4 ppm patent related to -CH- (-CH-CH_2-), another signal at 6.7 and 7.6ppm doublet

related to C-H aromatic due to presence of OH group (in ionized form)on position no.4 of aromatic ring, at 10.0 ppm related to OH group, as shown as in Scheme 5

^{1} H-NMR Spectrum VS.PVB

The more characteristic signals of VS.PVB compound showed as the following, triplet signal at 1.0 ppm related to protons of -CH_2- group, 3.4 ppm patent related to -CH- (-CH-CH_2-), another signal at 7.5-8.0 ppm related to aromatic ring, at 10.0 ppm related to OH group, and showed singular signal at 1.8 ppm related to Si-$(CH_3)_3$. Scheme 2

Antibacterial activity

All synthesized compounds were evaluated against certain kinds of Gram-positive bacteria (S. aureus) for their antibacterial activity, and Gram-negative bacteria (E. coli) and Klebsiella used the diffusion technique of the filter paper disk, measuring the diameter of the inhibition area after 24 hours. The preliminary findings showed that there were some active compounds against E. coli or and S. aureus, as shown in Table 3.

Most compounds prepared showed bacterial activity against Gram-negative and Gram-positive bacteria. Compounds PVB, VS.PVB, F.PVB, OCH_3.PVB and OH.PVB show good bacterial activity against (Staphylococcus aureus), and also had good activity against resistant bacteria Pseudomonas aeruginosa. The compounds showed good bacterial activity at high concertation against Gram-negative (E. coli), Klebsiella, and Gram-positive (S. aureus). Table 3. (Ali *et al.*, 2001)

Wound Dressing

New Zealand white rabbits were used in the study as 5 groups; each group consists of 6 animals (males 3) and (females 3). Animals were individually housed and were maintained at 19 $\pm$ 3 ºC with relative humidity at 30- 70%, a minimum of 10 to 13 complete air exchange per hour, and 12 hrs. Light/ dark cycle using full-spectrum fluorescent lights. The test and the control sites were prepared by clipping the skin of the trunk free of hair. Two application site on each animal was abraded by making open wound 8mm through the epidermis.

One site (A) was applying with the prepared compounds. The second (B) covered with controls. Animals were observed for signs of erythema and edema at 24 and 72 hours post-application of products. The animals in 4 groups were treated by introducing a thin film of the viscous oily PVB, F.PVB, OCH_3.PVB, OH.PVB at site A and povidone-iodine 10% at another site. The last group treated with VS.PVB at A site and silicone gel as control at B site. As shown in Table 4. (Estlander *et al.*, 1986)

Animals were observed daily for clinical manifestations. The erythema and edema for intact skin and abraded skin were observed as a function of time.

The signs and symptoms were observed after 24 hrs and 72 hrs. No erythema, no edema notes at the site of application of our compounds in the first 4 groups while the control site with povidone-iodine showed erythema and slightly edema during the first 24 hrs without edema.

The fifth group treated with VS.PVB, notes erythema slightly but not observed any signs at the site of control applied with silicone gel.

After 1 week from the application (twice daily), the healing was obtained completely for open wounds from PVB and VS.PVB compounds and without scare rather than the povidone-iodine and silicone gel, while the healing with other compounds occurs after 10 days without any scar. (Barrionuevo *et al.*, 2015)

CONCLUSION

New derivatives from polyvinylpyrrolidone and polydimethylsiloxane polymers were prepared as wound dressing has good antibacterial activity against gram-positive and gram-negative bacteria and very good effects in the treatment of open wounds during the short duration in comparison with commercial products.

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