Preparation of Polyvinyl Alcohol Hydrogel Through the Selective Complexation of Amorphous Phase

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ABSTRACT: Several methods for the preparation of polyvinyl alcohol (PVA) hydrogel are being reported in the literature. In this communication a new, simple, and mild complexation reaction using phenyl boronic acid, leading to a highly elastic PVA hydrogel, is addressed. It is found that the inherent crystalline property of the semicrystalline PVA is retained by the complexation reaction, which is confined to the amorphous region. An enhanced mechanical property, particularly in the wet condition, is observed after the modification resulting from the intact crystallinity. Also, the inherent nontoxic characteristic property of PVA is unaffected upon this complexation reaction. © 2001 John Wiley & Sons, Inc. J Appl Polym Sci 82: 143–149, 2001

Key words: polyvinyl alcohol; phenyl boronic acid; glutaraldehyde; crystallinity

INTRODUCTION

Hydrogels prepared by crosslinking of natural or synthetic polymers have a unique position in medical, pharmaceutical, and related fields because of their high water uptake. Crosslinked polyvinyl alcohol (PVA) as a hydrogel has attracted considerable attention because of its high degree of swelling in water, inherent low toxicity, good biocompatability, and desirable physical properties. Moreover, PVA has been extensively studied as a membrane in various ways because of its good film-forming and chemical-resistant properties. The material has figured in several studies as a drug-releasing matrix.

PVA can be crosslinked by different physical or chemical methods to give rise to the formation of hydrogel. Peppas and Merrill[1] investigated the crosslinking of aqueous PVA solution by electron beam or γ-irradiation. The method by which the PVA hydrogel is obtained through repeated freezing and thawing PVA solution has proven successful.[2] Photocrosslinking has also been attempted by introducing a styrylpyridinium group onto PVA and simultaneous exposure to UV light.[3] Chemical methods by adding crosslinking agents having bifunctional compounds such as, for example, boric acid, dialdehydes, dicarboxylic acids, dianhydrides, acid chlorides, and epichlorohydrin have also been used for preparing PVA hydrogel.[4–8] Some of these methods, although useful for the preparation of hydrogel, affect bioactive agents such as protein and enzymes during their incorporation into the PVA matrix.

Kitano et al.[9] demonstrated a glucose-sensing polymer complex system of boronate–diol interaction by the formation of a covalent complex between PVA and poly(*N*-vinylpyrrolidone) derivative having a phenyl boronic acid moiety. This communication addresses the morphological changes in PVA upon complexation with phenyl boronic acid and possible applications in the biomedical and pharmaceutical fields are speculated.

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EXPERIMENTAL

Materials

Hot water–soluble polyvinyl alcohol (S. D. Fine Chemicals, Mumbai, India) used for the studies was characterized by a degree of polymerization of about 300, with a degree of hydrolysis of 98.5–100% and viscosity of 4–6 cP at 20°C for 4% aqueous solution. Phenyl boronic acid (PBA) was obtained from Sigma Chemicals (St. Louis, MO). Glutaraldehyde of laboratory-grade reagent (25% w/v aqueous solution) and sulfuric acid were obtained from S. D. Fine Chemicals.

Methods

PVA films of 0.3 mm average thickness were prepared by casting aqueous solution of the polymer (10 g %) on a leveled glass tray, which was allowed to evaporate at room temperature (~ 30°C). Once the film dried it started to separate from the glass surface. At this stage, the film was peeled off from the tray and was used for studies after vacuum drying at room temperature (~ 30°C).

Treatment with Phenyl Boronic Acid

The films were exposed to phenyl boronic acid solution (5 g % by weight of PVA) in distilled water (DW) or 1 : 1 ethanol/DW mixture for 4 h. The films were then rinsed with DW thoroughly and dried at 50–55°C under vacuum in a vacuum oven.

For a comparison, glutaraldehyde (equivalent amount to that of PBA) crosslinked PVA films were also prepared according to the procedure reported elsewhere.[10] Briefly, 1 mL of glutaraldehyde was added to 100 mL of 0.1*N* sulfuric acid. Approximately 3 g of PVA film of 0.3 mm thickness were exposed to the acidic glutaraldehyde solution for 4 h. The film was then rinsed repeatedly in DW and was dried at 50–55°C under vacuum.

Equilibrium water content (EWC) was examined at room temperature (~ 30°C) by repeatedly weighing water-immersed samples of known initial weight at definite intervals. The percentage EWC was calculated by the equation

$$\text{EWC, in } \% = (W_2 - W_1) \times 100/W_2.$$

where W_1 is the dry weight (g) and W_2 is the swollen weight (g).

The attenuated total internal reflection (ATR) spectra of the materials were recorded using a Nicolet model Impact 410 FTIR spectrophotometer (Nicolet Instruments, Madison, WI) with a horizontal ATR accessory and a zinc selenide crystal.

An Instron universal testing machine (model 1193; Instron) was used for estimating ultimate stress and strain parameters of the polymer according to ASTM D-882. The crosshead speed was 100 mm/min.

Octane contact angles under water were measured on water-equilibrated samples with the help of a goniometer (Kernco Instruments, El Paso, TX).

The surface morphology of the films was examined using a scanning electron microscope (model S-2400; Hitachi, Japan). Samples were mounted on metal stubs using double-sided adhesive tape, gold-coated under vacuum, and then examined.

Differential scanning calorimetric studies were carried out on a TA Instruments DSC model 2920 (TA Instruments, New Castle, DE) in hermetically sealed aluminum pans under N_2, at a heating rate of 10°C/min up to 250°C.

X-ray diffusion studies were performed on a Siemens D5005 X-ray diffractometer (Siemens Medical Systems, South Iselin, NJ). A CuK_α line was used at a scan rate of 0.1° at room temperature. Polymer in the form of films was used for the studies.

The modified film was sterilized by γ-irradiation and was subjected to cell culture studies using L929 cells (mouse fibroblasts received from NCCS, Pune, India) for the cytotoxicity evaluation. Samples (~ 1 cm^2) were placed directly in contact with the cells. Morphology of cells was assessed using phase-contrast microscopy in comparison with control cells.

RESULTS AND DISCUSSION

Because phenyl boronic acid is water soluble, the complexation with PVA is found to occur rapidly under mild conditions. While exposing dry PVA films in an aqueous solution of PBA, we could not get a uniform film because of the high degree of swelling in the medium. Very good uniform films resulted when a mixture of ethanol/water (1 : 1) containing PBA was used.

Figure 1(a) and (b) show ATR–FTIR spectra of the control and modified PVA films, respectively. Upon modification there is reduction in intensity

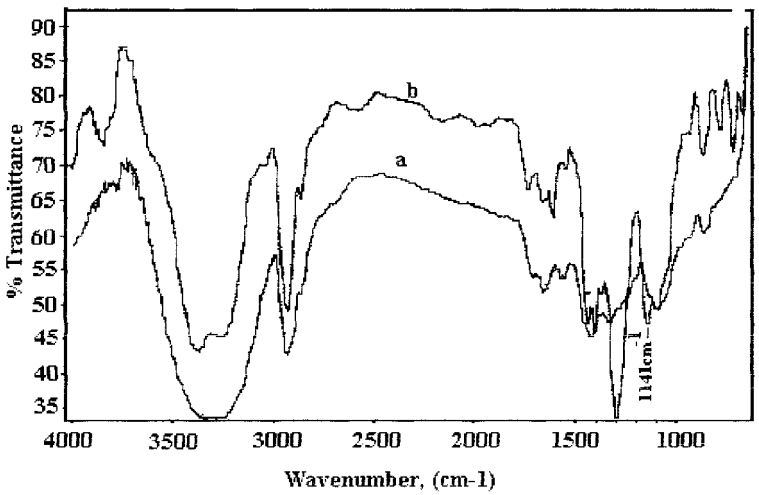


Figure 1 Typical ATR–FTIR spectra of polymer films: (a) control PVA; (b) PVA treated with PBA under ethanol/water medium.

of –OH bands around 3500 cm^{-1} and the appearance of a peak at 1300 cm^{-1} associated with B–O linkage in the treated films indicates the complex formation.

Table I summarizes the percentage equilibrium water content (EWC), the mechanical properties (both dry and wet), and octane contact angle data of the control and modified samples. The equilibrium water content and the wet strength of control PVA could not be measured because of handling problems resulting from the very high degree of swelling. In the case of modified samples the water equilibration attains within 15 min of exposure to water. Unlike the conventional method of glutaraldehyde crosslinking, the mechanical integrity of PVA is not altered considerably upon PBA complexation reaction under aqueous conditions. The percentage elongation of the dry samples after modification is more or less the same and is comparable to that of the control sample. While the medium for complexation is changed to 1 : 1 ethanol/water mixture, the ultimate stress is significantly reduced in a manner similar to that of the glutaraldehyde crosslinked sample, which is probably attributable to more complexation reaction under this medium. However, the percentage elongation is found to be unaffected. Compared to glutaraldehyde-treated PVA, phenyl boronic acid–complexed PVA can be considered superior in terms of mechanical properties (both wet and dry conditions) for elastic hydrogel applications. Octane contact angle data show that there is a relative reduction in hydrophilicity to the phenyl boronic acid–treated films. This is as expected because of the attachment of

Table I Stress–Strain Parameters, Equilibrium Water Content (EWC), and Octane Contact Angle

			Dry Samples		Wet Samples	
Sample	EWC	Octane Contact Angle (°)	Ultimate Stress (kg/cm^2)	Strain (%)	Ultimate Stress (kg/cm^2)	Strain (%)
Control PVA	—	151.5 ± 1.1	417.4 ± 16.4	406.0 ± 38.13	—	—
PVA–Gl[a]	38.5 ± 0.4	141.8 ± 2.8	222.9 ± 42.2	123.13 ± 35.1	22.46 ± 8.1	40.0 ± 12.2
PVA–PBA aqueous	57.5 ± 1.2	137.5 ± 1.1	441.4 ± 42.2	386.9 ± 83.0	13.82 ± 2.56	375.0 ± 35.7
PVA–PBA EtOH/H_2O	52.83 ± 1.5	133.0 ± 1.2	296.5 ± 32.9	368.0 ± 86.6	45.7 ± 6.8	533.3 ± 28.6

[a] PVA–Gl–PVA crosslinked with glutaraldehyde.

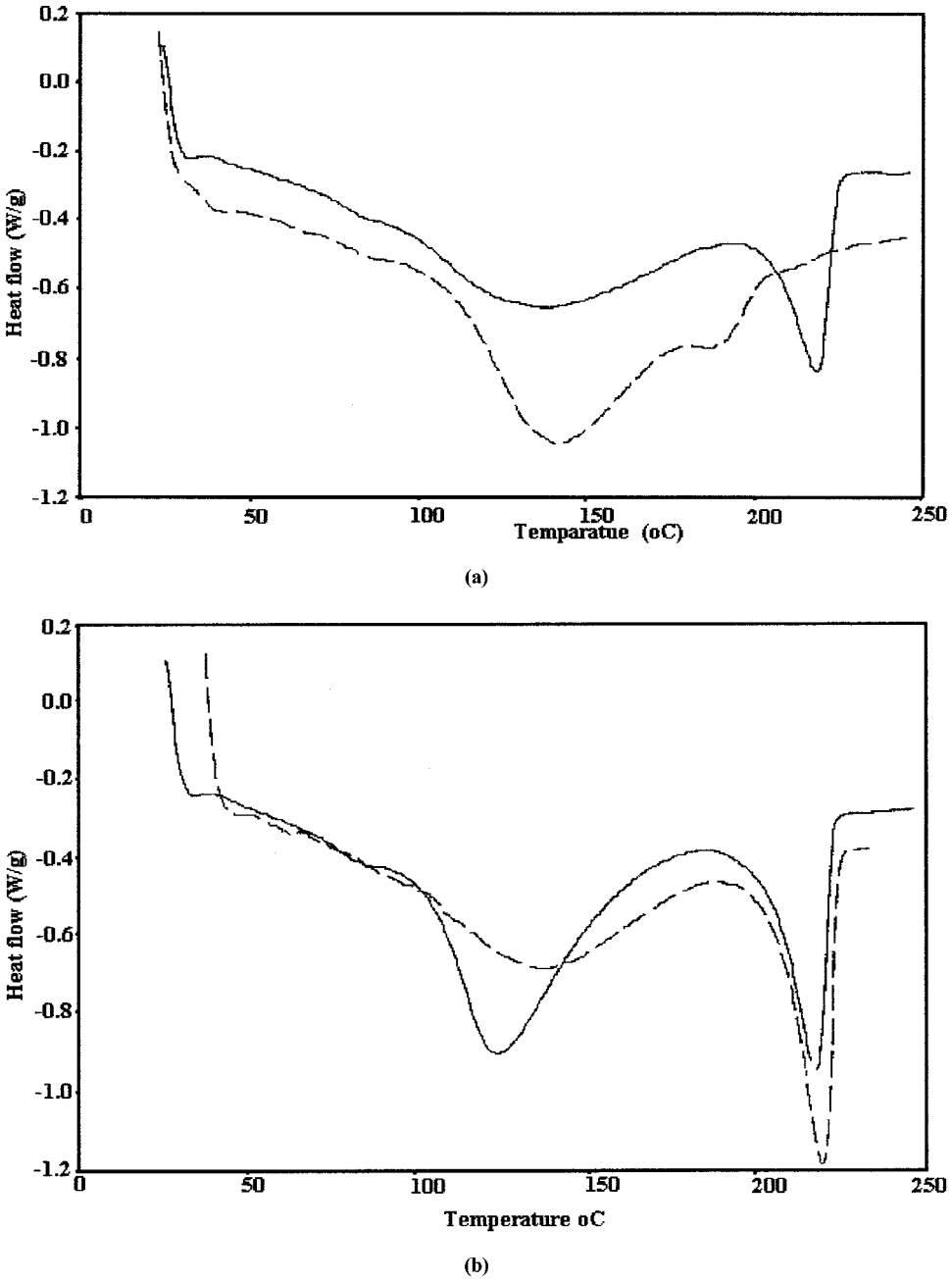


Figure 2 (a) DSC thermogram of control PVA (—) and glutaraldehyde-treated PVA (—). (b) DSC thermogram of PVA treated with PBA under aqueous condition (—) and ethanol/water medium (—).

hydrophobic phenyl groups onto PVA during the modification.

Figure 2(a) and (b) illustrate the differential scanning calorimetry thermogram of both the control and modified PVA samples. The broad endothermic peak with a peak maximum of about 120°C is present in all the cases and is attributed to the traces of water in the samples. The peak maximum temperature and the endothermic heat flow of the control and modified samples are tabulated separately (Table II). The second peak with a maximum around 218°C is associated with the melting of the polymer.

PVA is a semicrystalline polymer and the crystalline phase is associated with syndiotactic, atactic, or isotactic configuration. The melting point

Table II Data on DSC Studies

Samples	Melting Temperature Peak Maximum (°C)	Endothermic Heat Flow (W/g)
Control PVA	218.99 ± 0.59	43.51 ± 3.51
PVA–Gl	191.33 ± 1.8	8.28 ± 1.8
PVA–PBA aqueous	217.33 ± 0.48	51.13 ± 2.0
PVA–PBA EtOH/H_2O	216.8 ± 0.59	51.53 ± 3.52

around 218°C apparently indicates that the crystalline phase in the present case is isotactic.[11] In the case of the PBA-modified sample this peak seems to be more sharpened. As a result of the complexation it is assumed that the randomly distributed crystalline entities are segregated to get sharp melting characteristics. In a semicrystalline polymer, the randomly dispersed crystallites may have different environments, thus leading to a broader melting peak, although the glutaraldehyde-treated (PVA–Gl) polymer shows less crystallinity as a result of the crosslinking reaction (the crystallinity will virtually be lost with the extent of crosslinking). Assuming more complex formation with PBA under ethanol/water mixture based on the reduced ultimate stress and more hydrophobic surface (Table I), the DSC studies would have behaved in a manner similar to that of the glutaraldehyde-treated PVA sample. The reversal of this phenomenon possibly indicates that the complexation reaction is confined in the amorphous region, without affecting the crystalline phase.

Figure 3 illustrates the wide-angle X-ray diffraction traces of the PVA samples. Control PVA [Fig. 3(b)] shows a relatively sharp peak centered around a diffraction angle (2θ) of 19°. It is apparent that this reflection is associated with the crystalline phase present in PVA, which is already well known. The relative broadness of the trace

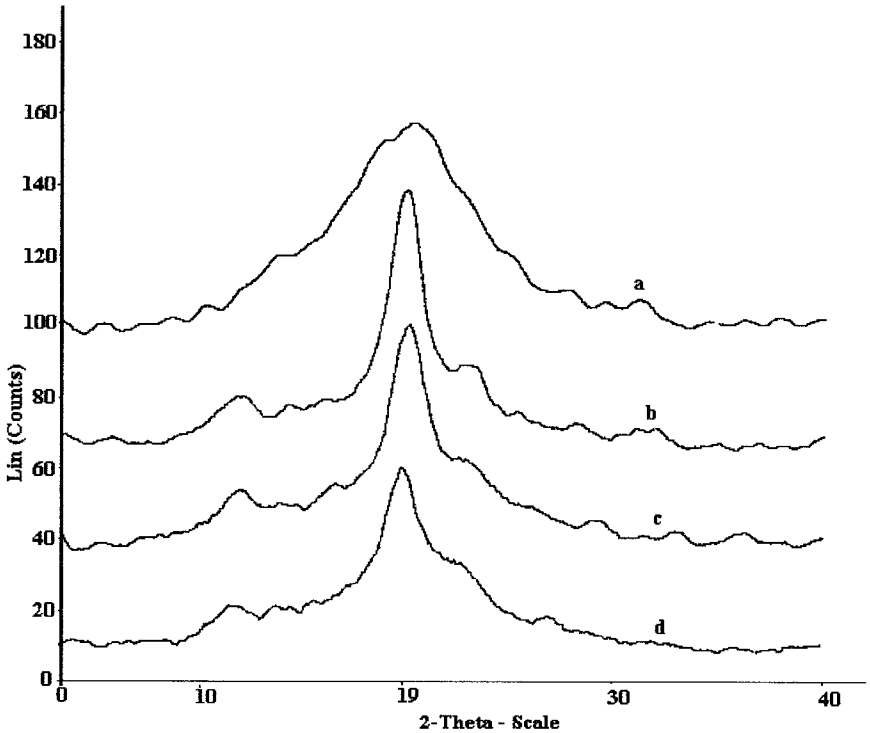
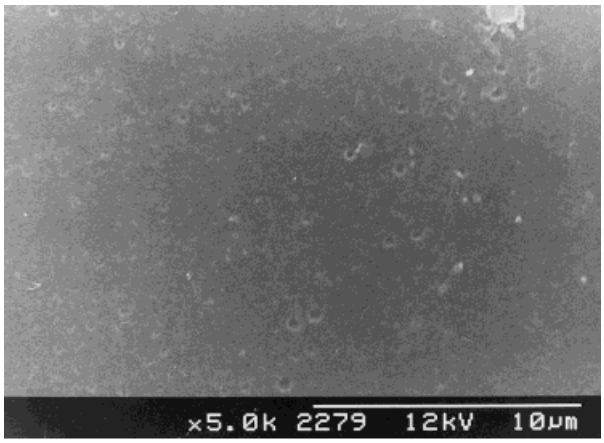


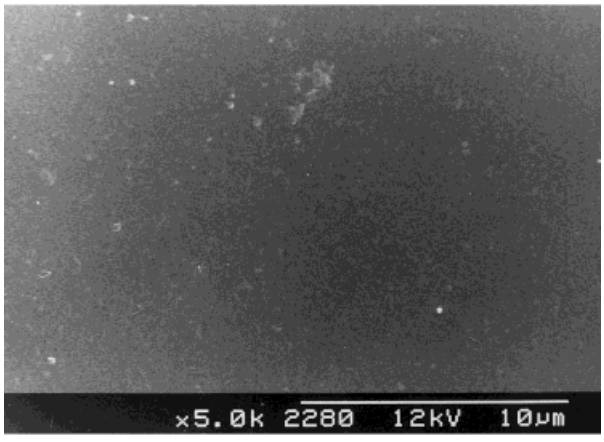
Figure 3 Wide-angle X-ray diffraction traces of polymer films: (a) glutaraldehyde-treated PVA; (b) control PVA; (c) PVA treated with PBA under ethanol/water medium; (d) PVA treated with PBA under aqueous condition.

possibly indicates that the crystalline phase contains crystallites of various sizes. The modified PVA samples that are complexed with phenyl boronic acid in aqueous and 1 : 1 alcohol/water, respectively, interestingly show nearly the same diffraction pattern as that of the control PVA, reflecting that these two samples also contain more or less the same crystalline content [Fig. 3(c) and (d)]. The striking feature is the disappearance of typical crystalline reflection from PVA crosslinked with glutaraldehyde [Fig. 3(a)]. This sample shows only a featureless broad diffraction pattern typical of the amorphous phase.

From the combined results of DSC and X-ray diffraction, it is easy to conclude that the glutaraldehyde disrupts the crystalline phase and that the PBA complexation does not affect the crystallinity on PVA. It is reported that the characteristic amount of crystallinity in PVA is demonstrated by the absorbance at 1141 cm^{-1} in the IR spectrum.[12] It is apparent that the peak centered around 1141 cm^{-1} is more predominant in PBA-treated film than that in control PVA, which indicates that the crystalline phase in the PVA is unaffected by this complexation reaction [see Fig. 1(a) and (b)].

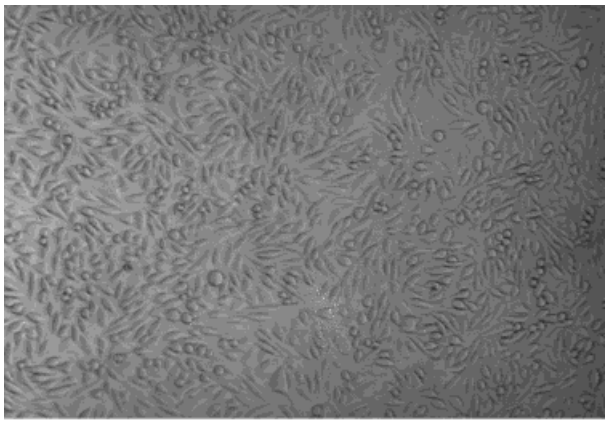


(a)

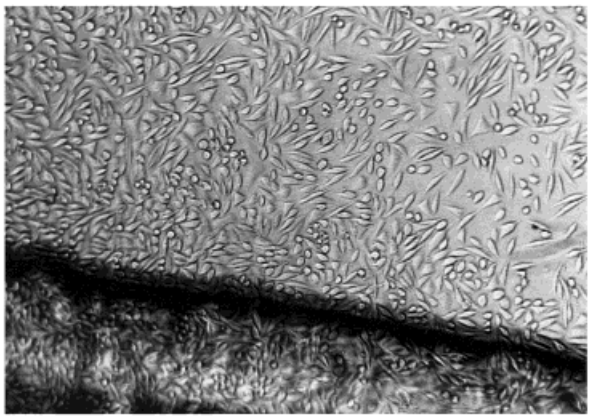


(b)

Figure 4 (a) Scanning electron micrograph of control PVA film. (b) Scanning electron micrograph of PVA film treated with PBA under ethanol/water medium.



(a)



(b)

Figure 5 (a) Phase-contrast micrograph of control L929 cells. (b) Phase-contrast micrograph of L929 cells in contact with PVA–PBA (treated under ethanol/water) polymer film.

The SEM photographs [Fig. 4(a) and (b)] show the surface morphology of PVA films, both control and modified ones. It shows that both surfaces are smooth and there is no alteration to the surface morphology during the modification.

Figure 5(a) and (b) show the morphology of the control cells and the cells in contact with the PBA-modified sample. It is evident that the morphology of the cells is unaffected and the nontoxic

characteristic of PVA is not altered upon this modification.

Because this complexation can be performed under mild aqueous conditions and will not leave behind a toxic residual, this modification method may have very good potential in the biomedical and pharmaceutical fields, especially for the encapsulation of bioactive agents, such as proteins, surface coating, liposome stabilization, as membranes and the like.

CONCLUSIONS

It can be concluded that the inherent characteristics such as crystallinity and noncytotoxicity of PVA are retained by the complexation reaction with phenyl boronic acid (PBA), which yields films of better mechanical properties than those of glutaraldehyde-crosslinked PVA films.

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