ASSESSMENT OF MANUFACTURABILITY AND PERFORMANCE OF POLYURETHANE HEART VALVES PRODUCED THROUGH A LOCALLY DEVELOPED DIP MOULDING PROCESS

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ABSTRACT

Polyurethane heart valves have been widely studied as possible replacement for mechanical and bioprosthetic heart valves. The development of an inexpensive routine production technique for manufacturing of polyurethane valves will greatly benefit a very large number of patients in developing and emerging countries. A polymer heart valve shows favourable physical properties and flow dynamics compared to human heart valves, however, the outcome of producing a polymer heart valve with the required flexibility, durability and hemodynamic function is often difficult to predict. The design of the mould, the selection of the material and the fabrication method used are the key factors that influence the achievement of an acceptable heart valve for use in the human body. From their previous work on developing a repeatable, semi-automated dip moulding process for producing tri-leaflet polyurethane heart valves, the authors have shown that the selection of an appropriate set of dip moulding process parameters and mould material properties could result in achieving polyurethane valve leaflets with the required physical and mechanical properties.

This paper reports on the progress made with application of the developed dip moulding process to produce polyurethane heart valves suitable for use in human body. The mould, frame and sewing ring were manufactured in Ti6Al4V(ELI) by using a Direct Metal Laser Sintering (DMLS) process and the valve leaflets were moulded directly onto the sewing ring. The heart valve properties obtained are presented and assessed. Conclusions are drawn regarding the prospects of these valves surviving the extensive in vitro simulation trials required to qualify them for subsequent clinical trials.

1. INTRODUCTION:

The replacement of cardiac valve can either be with biological or artificial valves. The biological heart valves experience a short fatigue life and suffer from calcification leading to failure. This results in multiple surgeries for their replacement bringing great discomfort in the life of the patient [1]. These shortcomings have been overcome by development of artificial heart valves, the practice which has been done for a period of more than six decades. It has been reported that commercially available mechanical heart valves suffer from thromboembolism and require anticoagulation treatment [2][3]. It is not always possible to monitor the level of anticoagulation properly since international normalized ratio (INR) clinics are not always in close proximity to patients especially in developing and emerging countries, and uncontrolled anticoagulation process can lead to internal bleeding within the heart[4][5].

Polyurethane heart valves have been widely studied as possible replacement for mechanical and bioprosthetic heart valves [6][7][8]. The development of an inexpensive routine production technique for manufacturing of polyurethane valves will greatly benefit a very large number of patients in developing and emerging countries. A polymer heart valve shows favourable physical properties and flow dynamics compared to human heart valves, however, the outcome of producing a polymer heart valve with the required flexibility, durability and hemodynamic function is often difficult to predict [3][9][10]. In collaboration with the Robert WM Frater Cardiovascular Research Centre, Department of Cardiothoracic Surgery, University of the Free State, initial experimental work was done to establish a process and a set of process parameters and conditions that would enable repeatable and reliable local production of tri-leaflet polyurethane heart valves. This represented only the first phase of the development process [11].

Intensive research has been performed in regards with the heart valve design, fabrication method and material selection [3][12][13]. Thermoplastic Polyurethane is Food and Drug Administration (FDA)-approved family polymer for cardiovascular devices. Thermoplastic Polyurethane is a biocompatibility polymer material with relatively good mechanical properties and good hydrodynamic function [3][13][14]. A commercial trade mark known as PC3595A is one of the series of Polycarbonate urethane which is a family of aliphatic and aromatic polycarbonate-based thermoplastic polyurethane. In this study PC3595A granules are dissolved through Dimethylacetamide (DMAc) solvent to obtain a solution to be used for dip moulding for fabrication of the polyurethane heart valves [11].

The fabrication methods have an important influence on the physical properties of the leaflets, the durability and hemodynamic function of polyurethane valves [3][9]. The human heart valve leaflets do not have uniform thickness. For the effectiveness of the hydrodynamic function of the valves, they are formed by membranes of various thicknesses along the axis of symmetry [15][8]. The dip moulding process was found to produce heart valve leaflets with thickness varying uniformly from the top edge (thinner) to the bottom edge where the maximum thickness is measured [11]. This is an advantage because the bottom thicker edge might provide a sealing function for a trileaflet valve and improve the durability of the valve. The research conducted at the University of Strathclyde found that for a good function of the heart valve, the leaflet thickness should fall in the 100 to 150 μm thickness range [16].

2. EXPERIMENTAL METHOD

A two-phased development approach was adopted for this project is:

- Phase 1: Establish an experimental set-up to determine dip moulding process variables that would result in controllable and reproducible polymer films with the potential to be used for heart valves.

- Phase 2: The dip moulding parameters developed during Phase 1 will be used with a heart valve mould to manufacture heart valves to be used for pulse duplication and, fatigue tests. These parameters will also serve as input for computational fluid dynamic modelling to identify potential design improvements.

Figure 1 illustrates the two-phased development approach diagrammatically. The FACILITY PREPARATION and PROCESS PARAMETERS stages in this diagram represent Phase 1, while the MOULD HEART VALVE LEAFLETS and the TESTING HEART VALVES stages represent Phase 2 of the development process.

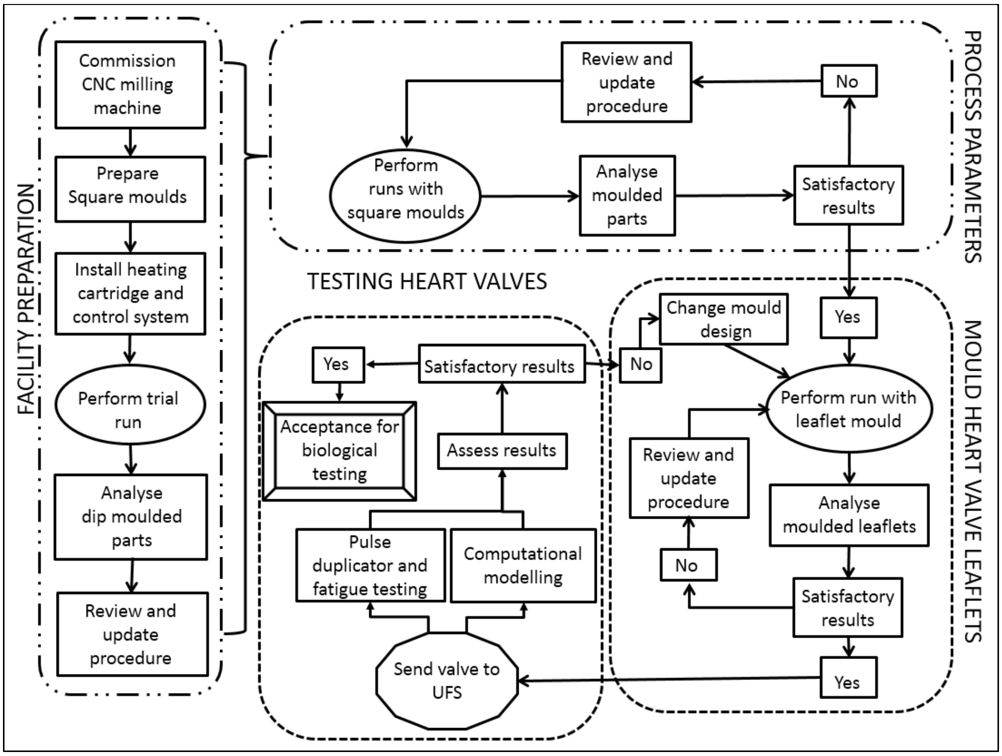

Figure 1: Representation of the two two-phased development approaches for a polyurethane heart valve

Phase 1 enclosed with (— · · — · · — · · — · ·)
Phase 2 enclosed with (- - - - - - - - - - - - - - -)

Phase 1 was completed successfully and the results were published in a previous article [11]. Key parameters that have an influence on producing acceptable films were established. These parameters include:

- The concentration of the polymer in the polymer-solvent solution,
- Dipping and withdrawal speed of the mould,
- Curing temperature,
- The number of dips.

The focus of the current study was on Phase 2, resulting in prototype polyurethane heart valves.

2.1 Mould

The mould geometry was prepared through a Direct Metal Laser Sintering (DMLS) process. Titanium alloy (Ti6Al4V) was selected due to its high strength and fatigue resistance. Polymer valves with an internal diameter of 19 mm were produced through multiple dipping.

2.2 Solution preparation

To manufacture a dip moulded polymer heart valve, a solution of polyurethane (PC3595A clear) were dissolved in a solvent (DMAc). The viscosity of the solution depends on the solids contents, which can be altered by adding more solvent or polyurethane material to the solution until the desired consistency is obtained. A 20% w/w solution was prepared as referred to in previous work.

2.3 Dip moulding process

The automated dipping and coating procedure making use of a CNC machine, facilitated a smooth and controlled movement of the mould. The mould is lowered at a controlled speed into the polymer solution to minimize air bubbles which can result in fatigue failure of the finished product and a more even thickness distribution across leaflets. The mould was removed from the CNC machine with a thin coating after each dipping, excess polymer solution was allowed to drain. The mould was then placed in an air circulating oven at 25°C temperature for an hour to remove solvent, dimethylacetamide (DMAc). The leaflet form as the solvent evaporates and a thin surface of polymer remains on the mould. This process was repeated until the required thickness was obtained. The dip moulded leaflets are released from the mould manually.

3. RESULTS AND DISCUSSION

Different parameters of dip moulding process were evaluated. The Figure 2 shows influence of each parameter on producing acceptable polyurethane heart valve.

3.1 Dipping speed

With three dips, the dipping speed was varied from 2 to 79 mm/min. The highest dipping speed was found to display a higher number of air bubbles (Figure 2A) which consequently will lead to early failure of the valve. The lowest dipping speed resulted in significant reduction of air bubbles (Figure 2C) but did not completely eliminate them.

Figure 2F shows a valve produced from a single dip with no air bubbles entrapped. This indicates bubbles are trapped during second and third dips. The CNC machine’s movement, used for this review can be as slow as 2 mm/min, with the existence of air bubbles on the second and third dip as a results of accumulating a required thickness concludes for another parameter to be assessed to eliminate this barrier for a durable valve.

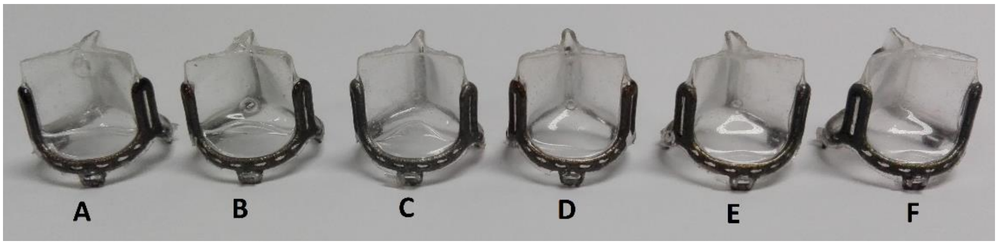

Figure 2: Sample of the valves produced with different dip mould parameters

3.2 Preheating temperature, solution concentration and withdrawal speeds

At room temperature, PC3595A granules were found partially dissolving with DMAc solvent. When the temperature of both mould and polymer solution was raised up to 90ºC, it was observed that a homogeneous solution was obtained. However, the preheating process of the mould and the solution resulted in about 15% decrease of the thickness of the heart valve leaflets in such a way that the newly obtained thicknesses became less than the minimum acceptable heart valve leaflet thickness.

To increase the thickness, the withdrawal speed was raised from 20 to 790 mm/min. As this effect was also found by other researchers [17][18]. Figure 3 shows a valve produced with a higher concentration polymer-solution, when the mould and polymer solution were preheated at 90ºC with a single dip at a lower dipping speed and a higher withdrawal speed.

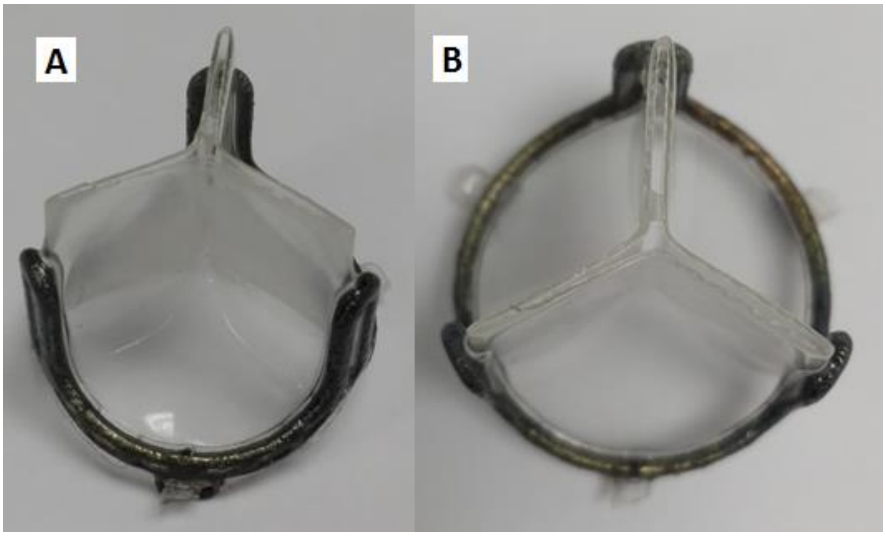

Figure 3: Tri-leaflet PU valve produced with dip moulding process without final trimming

- **(A) Side view of the valve**
- **(B) Top view of the valve**

The thickness of the obtained heart valve leaflet was measured at different locations of the leaflets as indicated by the Figure 4.

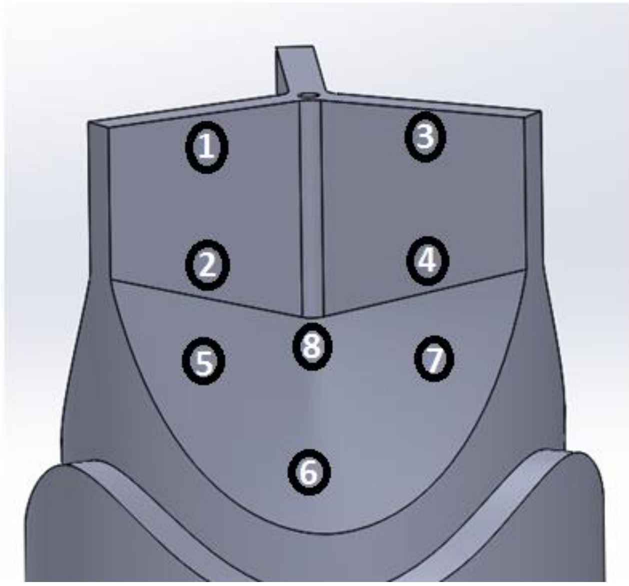

Figure 4: Representation of the tri-leaflet polyurethane valve thickness measurements

The results of the measured thickness are presented in Table 1

Table 1: Thicknesses of the polyurethane leaflets in a high concentrated polymer solvent solution

Measured location	1	3	2	4	5	7	6	8
Thickness (µm)	198±16	173±16	82±9	89±4	91±20	95±23	98±6	85±8

The ideal objective is to obtain the thickness measured at locations 2 and 4 and at locations 5 and 7 with a difference not more than 10 µm. From Table 1, it can be observed that this objective has been achieved. However, the measured thicknesses are less than 100 µm which is the minimal thickness required for durability of heart valve leaflets.

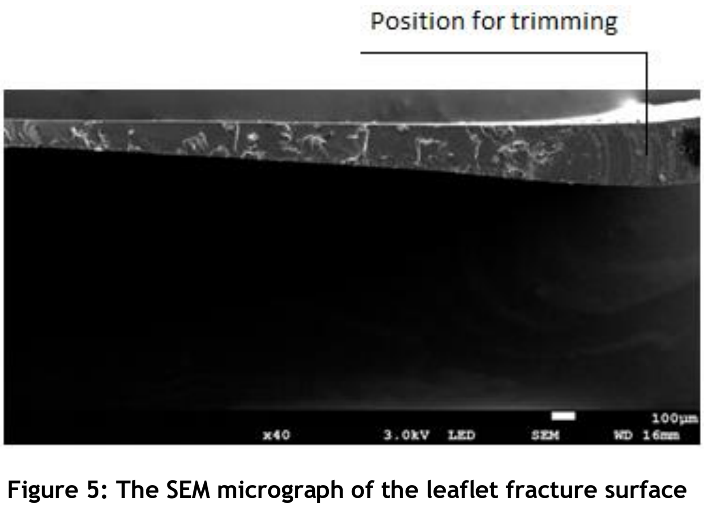

Figure 5: The SEM micrograph of the leaflet fracture surface

Furthermore, the thickness measurement taken at location 1 and 3 on the upper area of the tri-leaflet valve is greater than 150 µm, which is the maximum thickness for a good hydraulic function of the heart valve leaflets. However, in practice this area is eliminated by trimming, from the integral operational part of the heart valve leaflets. The Scanning Electron Microscope (SEM) was used to assess the variation of the thickness in vertical direction. The minimal thickness was found to be 76 µm at the lowest edge of the heart valve leaflets while the maximum value was 249 µm at the upper edge of the heart valve leaflets. This correlates with the previous findings where it was mentioned that the thickness varies linearly from lower edge with minimum value to the upper edge with the maximum thickness [11].

3.3 Surface topography of polyurethane leaflets

It is desirable that both sides (the side facing the mould and the side facing away from the mould) of the leaflets reflect more or less same surface topography. The used mould has six vertical flat and three upper curved surfaces (Figure 4). It was observed that for all vertical flat and curved surfaces, the leaflet sides facing away the mould displayed more or less same surface topography (Figure 6 A & C). The same trend is also observed with the sides facing towards the mould (Figure 6 B & D). This showed that the polishing technique of the flat vertical and the curved surfaces produced the same quality of surface finish. However, the sides facing away the mould (Figure 6 A & C) appeared with smoother surface topography than the sides facing towards the mould where uneven surface topography is dominating (Figure 6 B & D).

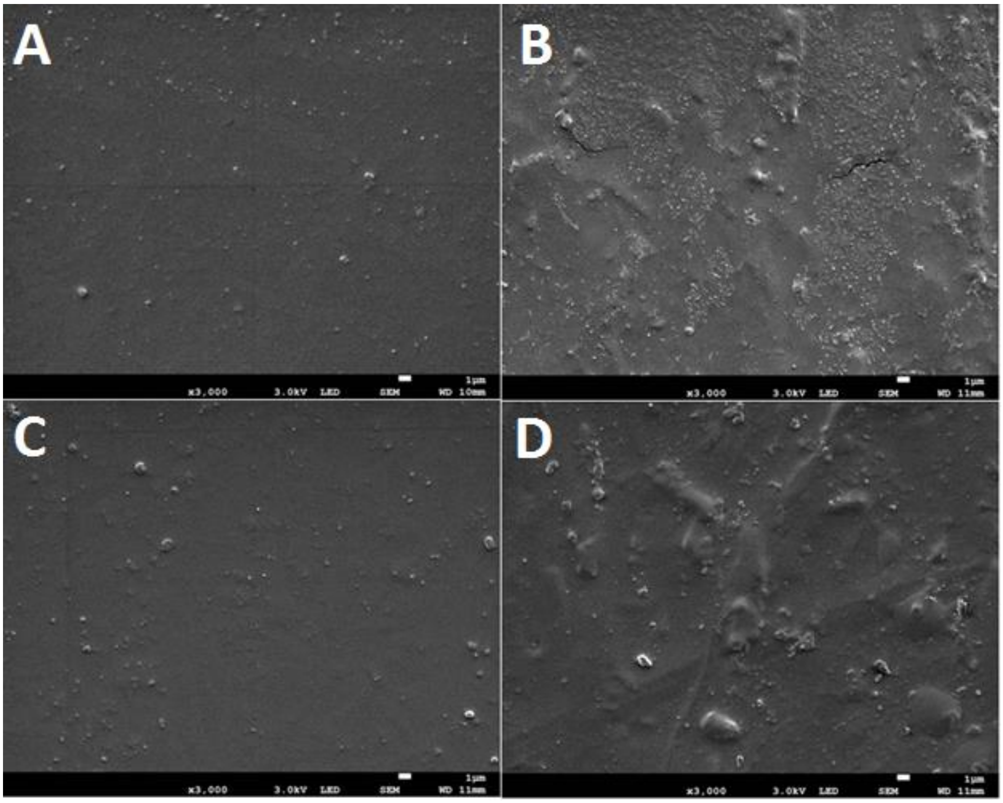

Figure 6: SEM micrographs of polyurethane leaflet surface topography for different faces

- **(A) Flat surface of the mould facing away from the mould**
- **(B) Flat surface of the mould facing towards the mould**
- **(C) Curved surface of the mould facing away from the mould**

(D) Curved surface of the mould facing towards the mould

The cross-section of the polyurethane leaflet deposited with the dip moulding method is displayed in Figure 7. The absence of pores in the cross-section of the leaflets is quite clear.

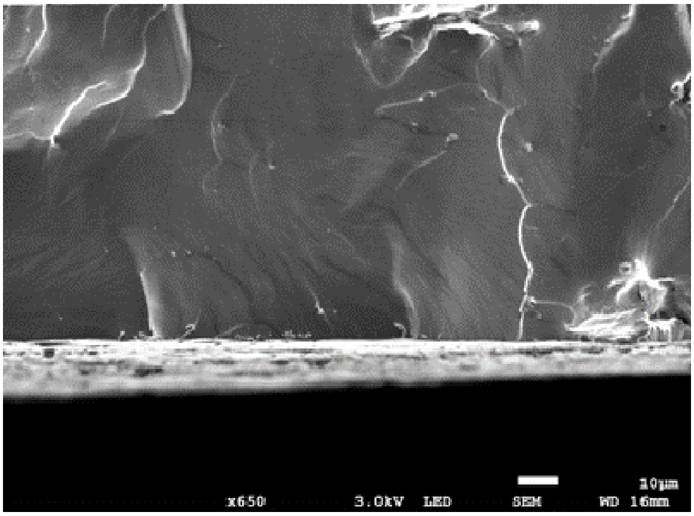

Figure 7: SEM micrograph of the fracture surface of a leaflet produced with a single dip TPU solution.

One of the first heart valve prototype manufactured was tested on a pulse duplicator machine. The machine had the feature to capture an operational video of the valve. Figure 8 illustrates a tri-leaflet polyurethane valve displaying the functionality of the valve during testing inside the pulse duplicator. This is just a visual indication of the valve's functionality. Quantified data on the valve's performance and lifespan, using the pulse duplicator test, will be collected by the Robert WM Frater Cardiovascular Research Centre, Department of Cardiothoracic Surgery, University of the Free State.

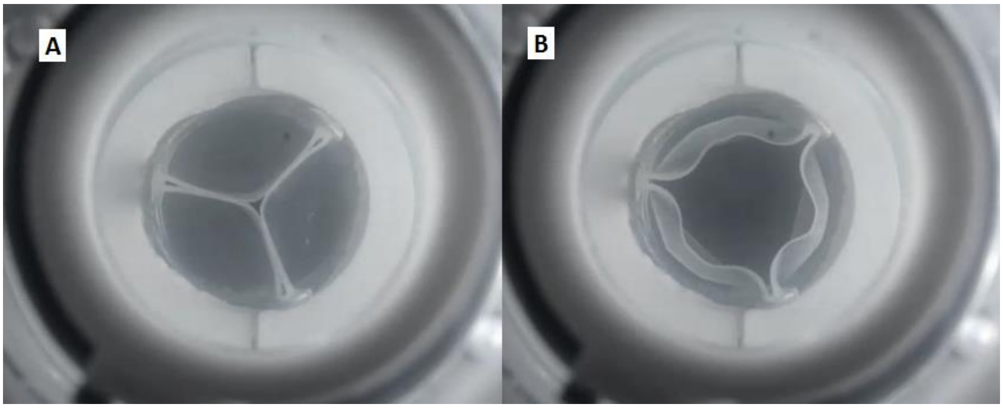

Figure 8: Polyurethane heart valve captured from the fatigue testing video

- **(A) Valve fully closed**
- **(B) Valve fully opened**

The team from Robert WM Frater Cardiovascular Research Centre, indicated that from visual observation of the valve operational functionality, being able to fully close (Figure 8 A) lead to the success of acceptable heart valve for use in the human body.

4. CONCLUSION

- A trileaflet heart valve prototype was successfully produced by dip moulding method with promising dynamic and durability functionalities.
- With a solution concentration varying from 20 to 30%, a single dip could produce a trileaflet heart of valve with a thickness varying from 76 to 249 μm in different locations of the heart valve leaflet.
- An excellent surface topography without air bubbles was achieved using a lower dipping speed.
- Future work will focus on quantitative study of pulse duplicator test results as well as tensile and fatigue tests.

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