

Magnesium Alloy: A Biomaterial for Development of Degradation Rate Controllable Esophageal Stent

Li Hong Chen, Wei Zhou, Chu Sing Lim, Eng Kiong Teo, and Ngai Moh Law

Abstract—Magnesium alloy has been widely investigated as biodegradable cardiovascular stent and bone implant. Its application for biodegradable esophageal stenting remains unexplored. This paper reports the biodegradation behaviors of AZ31 magnesium alloy in artificial saliva and various types of beverage *in vitro*. Results show that the magnesium ion release rate of AZ31 in artificial saliva for a stent (2cm diameter, 10cm length at 50% stent surface coverage) is 43 times lower than the daily allowance of human body magnesium intakes. The degradation rates of AZ31 in different beverages could also be significantly different. These results suggest that the esophagus in nature is a less aggressive chemical environment for degradation of magnesium alloys. The significant difference in degradation rates of AZ31 in different beverages opens new opportunities for development of degradation controllable esophageal stent through customizing ingested beverages.

Keywords—Biodegradable esophageal stent, beverages, magnesium alloy, saliva.

I. INTRODUCTION

THERE are increasing interests to use stents for treatment of various kinds of benign esophageal conditions [1]. The wide spread of the stents for treatment of benign esophageal conditions however are restricted. The permanent metallic stents have low delivery profile, good mechanical strength and resistance to migration; however, they are difficult to remove. The permanent plastic stents are easy to remove. However, they are bulky to delivery and are easy to migrate, requiring a second surgery for stent removal. In recent years, biodegradable polymer based esophageal stents become available. Those stents however are prone to migration and are bulky in size due to intrinsic limitation of the material [2], [3].

Magnesium alloy is a class of metallic based biodegradable material which has been shown to have good biocompatibility [4], [5]. It possesses higher mechanical strength than the biodegradable polymer. This allows manufacturing of smaller stent profile with adequate mechanical properties. At gastrointestinal tract, the alloying elements will only be fractional absorbed [6]. This allows a more flexible selection of magnesium alloys without exceeding upper tolerance intake

level. Moreover, the esophagus is an open-ended tube. Hydrogen gas generated during degradation of magnesium alloy can be easily expelled out through belch. Due to the above advantages, it is hypothesized that the magnesium alloys could be used for development of biodegradable stent for temporary esophageal stenting.

In the development of biodegradable magnesium based esophageal stent, an essential step is to understand the biodegradation behaviors of the magnesium alloys in esophagus [7]. As it is known, esophagus is a muscular tube that connects the mouth to stomach for transportation of food and drinks. During non-meal time, the inner surface of esophagus is bathed with swallowed saliva and a thin aqueous bicarbonate-rich mucus layer. This makes esophagus an alkalinized environment in nature [8]. During meal time, the pH of esophagus may be transitorily changed associated with the pH of the ingesta. In this study, in order to define the property profile of the material for application, the degradation behaviors of one of the commonly used experimental alloy AZ31 was studied in artificial saliva and several commonly consumed beverages.

II. EXPERIMENTAL

A. Preparation of Samples and Testing Mediums

The rolled AZ31 magnesium alloy sheet with the following chemical compositions (in wt. %): Al-2.7, Zn-0.81, Mn-0.3, Fe-0.0035, Si-0.008, Cu-0.0026, Ni-0.0007, Ca-0.0032, Mg-balance) was used. Samples with dimensions of 10mm x 10 mm x 0.4mm were cut and ground up to 1200 grit SiC paper. After grinding, the samples were ultrasonically washed in ethanol for 10 minutes followed by drying at room temperature.

Table I lists the solutions and beverages used in this study. Their pH values and temperatures are included in the table. The artificial saliva was prepared as described in [9]. All chemicals used were reagent grades purchased from Sigma-Aldrich. All the beverages were purchased from local grocery store. The milk and orange juice, coca cola and sprite were kept in 4°C fridge after purchase and warmed up to room temperature in water bath prior to testing. Milo was prepared by following the description on product package and then cooled down to room temperature.

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TABLE I
SOLUTIONS AND BEVERAGES USED IN CURRENT STUDY

| Solutions and beverages | pH levels | Temperatures |
|-------------------------|-----------|--------------|
| Artificial saliva [9] | 6.8 | 37° |
| Milk | 6.67 | 23° |
| Fresh orange juice | 3.57 | 23° |
| Coca Cola | 2.39 | 23° |
| Sprite | 3.24 | 23° |
| Milo | 7.00 | 23° |

B. Immersion Tests

The immersion tests were conducted according to ASTM – G31-72. The pre-ground and cleaned samples with dimensions of 10mm x 10mm x 0.4mm were weighed and immersed in 45 ml testing solutions in 50ml centrifuge tube for two days under temperature as described in Table I. At the end of the test, the samples were cleaned by dipping in boiling 15% CrO₃ + 1% AgCrO₄ solution for 3min followed by ultrasonic ethanol cleaning in 99% ethanol. Average degradation rate was then calculated in mg·cm⁻²·day⁻¹ based on weight loss. The immersion tests were conducted triplicate to obtain reproducible results. To provide a reference, three samples were also immersed in simulate body fluid [10] at 37° for same period of time.

C. Electrochemical Tests

Potentiodynamic scanning was performed using a potentiostat/galvanostat corrosion measurement system (EG&G model 263A). A three-electrode cell kit (Model K0235 Princeton) with the specimen as the working electrode, an AgCl/Ag reference electrode as a reference electrode and the platinum electrode as the counter electrode was used. The exposed area was about 1cm². The potentiodynamic polarization test was carried out at a rate of 0.8mV s⁻¹ at 3 hours after immersion of samples.

D. Corrosion Morphology

To observe the surface morphologies of the samples after immersion test, the samples after cleaning were monitored by scanning electron microscopy (SEM, Joel Model 5600 LV).

III. RESULTS

The weight losses of the samples after two days of immersion were shown in Fig. 1. Results show that the degradation rate of AZ31 in artificial saliva is about 20 times slower than that in simulate body fluid. From the obtained degradation rate, the daily release of magnesium ions to the body based on a normal esophageal stent (20cm in diameter, 10cm in length with 50% of stent surface coverage), shall be around 16mg. This is around 43 times lower than daily allowance of magnesium intakes [11].

From Fig. 1, it is also seen that the degradation rates of AZ31 in milk and milo are slightly slower than in artificial saliva. The degradation rates in orange juice, sprite and coca-cola however could be up to 42 times higher than that in artificial saliva. The degradation rate in orange juice (the highest) is up to 64 times higher than that in milk (the lowest). A correlation of the degradation rates with the pH levels of the

studied fluids reveals that there are no correlation between the pH levels of the tested fluids and the degradation rates. Similar results were also reported in [12] where a dental alloy was shown to corrode differently in the different beverages independent of the pH levels of the beverages.

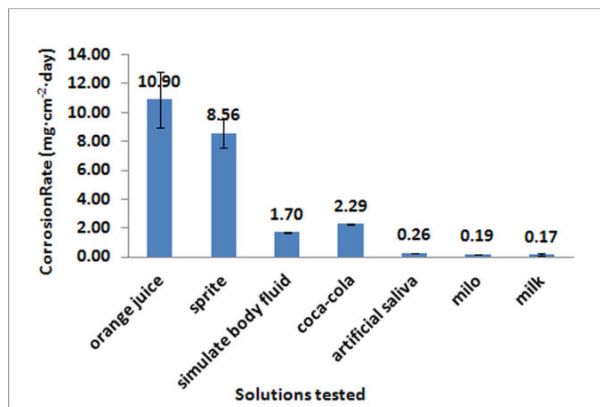


Fig. 1 Degradation rates of AZ31 Mg alloy in artificial saliva and different beverages

Fig. 2 shows the potentiodynamic polarization curves of AZ31 in artificial saliva, milo and milk. A passive region followed with an evident transpassive region is seen on all curves. The passive region however is not distinct. This indicates that the protective layer as formed on the sample surface cannot effectively inhibit the localized corrosion. The protective layer could easily break off leading to localized corrosion in those tested solution. Fig. 3 shows the potentiodynamic polarization curves for AZ31 samples in sprite, orange juice and coca cola. All curves show a rapid increase of current and early reach of maximum value at anodic branches. Concurrently occurred fast general and pitting degradation are indicated.

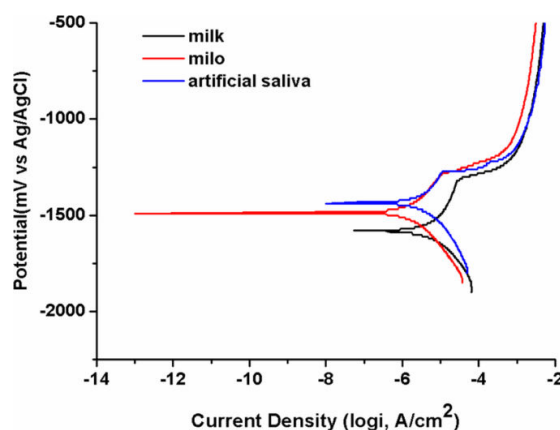


Fig. 2 Potentiodynamic polarisation curves for AZ31 in artificial saliva, milk and milo

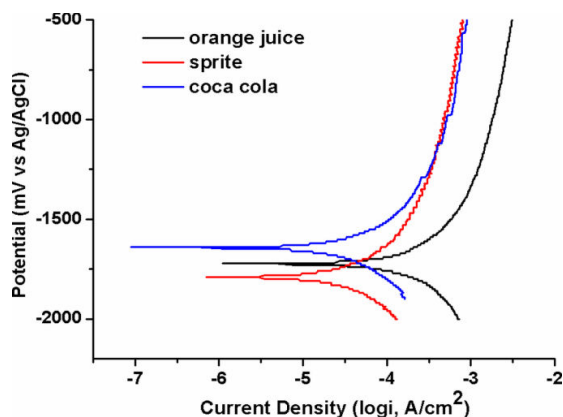


Fig. 3 Potentiodynamic polarisation curves for AZ31 in orange juice, sprite and coca cola

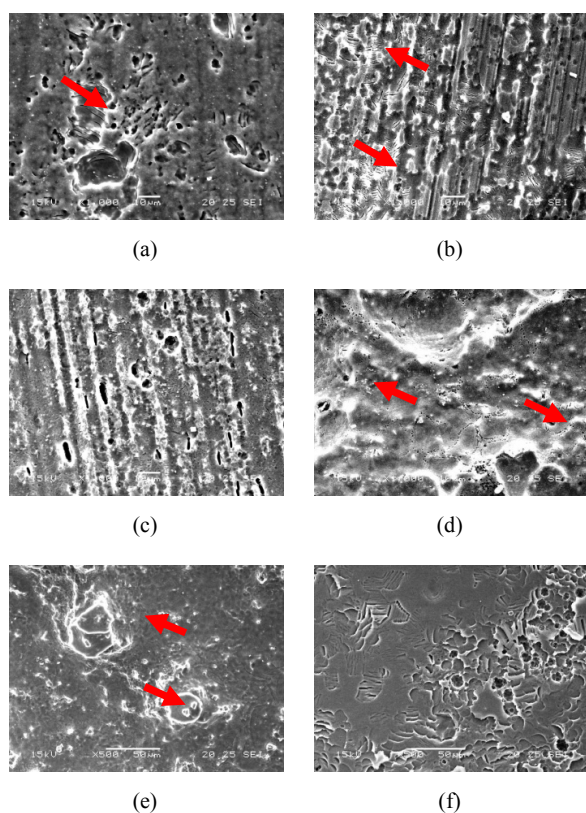


Fig. 4 Surface morphologies of the samples immersed in different testing solutions (a) artificial saliva (b) milk (c) milo (d) orange juice (e) sprite (f) coca cola

Fig. 4 shows the surface morphologies of the AZ31 samples in artificial saliva and different tested beverages. The surface morphologies of the samples are consistent with the potentiodynamic scanning findings. The surfaces of the samples immersed in artificial saliva, milk and milo show evident pitting with formation of corrosion pits or preferential corrosion at twins (arrowed). The surfaces of the samples immersed in orange juice are severely corroded with sporadically pitting holes (arrowed). The samples immersed in

sprite showed severely corroded surface with formation of “island like” regions (arrowed) due to preferentially corrosion around the second phases. The samples immersed in coca cola show homogeneously preferential corrosion around grain boundaries and formation of sporadical pitting holes.

IV. DISCUSSIONS

The magnesium alloys show great potential for development of biodegradable implants. In the development of biodegradable stents, the materials are however corroded too fast and are weaker in mechanical strength comparing to conventional metal biomaterials. These two shortcomings pose great challenge for designing a predictable performance stent to provide mechanical support at desirable period during tissue healing [13]. In clinical practices, there is a need of a better biodegradable stent especially for temporary esophageal stenting [2]. Despite of the need, there appears a lag in development of biodegradable stent due to much unknown clinical utility and requirement of an ideal design [1].

This paper for the first time investigate the biodegradability of a magnesium alloy at simulate esophageal chemical environment in vitro. Results show low degradation rate of AZ31 in simulate saliva which simulates the esophagus chemical environment during rest. This suggests that esophagus may in nature a less aggressive chemical environment for degradation of magnesium alloy due to lower contents of chloride ions, higher contents of phosphates and carbonates in the saliva than in blood plasma [14].

The degradation behaviors of AZ31 are also shown to be significantly different in different tested beverages. Due to the complexity of the compounds in each beverage, it is difficult to understand the effect of a particular component in each beverage in this paper. Nonetheless, some food compositions including casein, vitamin C, amino acids, starch had been shown could affect the corrosion [15] - [20]. Customizing the beverages for patients is viable for control of the degradation of the magnesium alloy.

V. CONCLUSION

This study has shown that esophagus in nature is a less aggressive chemical environment for degradation of magnesium alloys. Customizing the beverages for patients with magnesium esophageal stenting is viable for controlling the performance of the stent. Further interdisciplinary research for understanding the degradation behavior of the magnesium alloy in esophagus and quantifying the material property profile is needed for developing degradation controllable magnesium based esophageal stent.

REFERENCES

- [1] J. L. Tokar, S. Banerjee, B. A. Barth, D. J. Desilets, V. Kual, S.R. Kethi, et al., Drug-eluting/biodegradable stents. *Gastrointestinal Endoscopy*, 2011. 74(5): p. 954-958.
- [2] S. Irani. and R. Kozarek, Esophageal stents: past, present, and future. 2010. 12(4): p. 178-190.
- [3] P. Sharma and R. Kozarek, Role of esophageal stents in benign and malignant Diseases. *Am J Gastroenterol*, 2009. 105(2): p. 258-273.

- [4] X. Gu, Y. Zheng, Y. Cheng, S. Zhong, T. Xi, In vitro corrosion and biocompatibility of binary magnesium alloys. *Biomaterials*, 2009. 30(4): p. 484-498.
- [5] S. Schumacher, J. Stahl, W. Bäumer, J. M. Seitz, F. W. Bach, L. J. Petersen, Ex vivo examination of the biocompatibility of biodegradable magnesium via microdialysis in the isolated perfused bovine udder model. *International Journal of Artificial Organs*, 2011. 34(1): p. 34-43.
- [6] G. L. Diamond, P.E. Goodrum, S.P. Felter, W. L. Ruoff, Gastrointestinal absorption of metals. *Drug and Chemical Toxicology*, 1997. 20(4): p. 345-368.
- [7] F. Witte, N. Hort, C. Vogt, S. Cohen, K.U. Kainer, R. Willumeit, et al., Degradable biomaterials based on magnesium corrosion. *Current Opinion in Solid State and Materials Science*, 2009. 12(5-6): p. 63-72.
- [8] R. C. Orlando, Esophageal mucosal defense mechanisms. *GI Mobility online*, 2006.
- [9] J-Y. Gal, Y. Fovet, and M. Adib-Yadzi, About a synthetic saliva for in vitro studies. *Talanta*, 2001. 53(6): p. 1103-1115.
- [10] A. Loos, R. Rohde, A. Haverich and S. Barlach, In vitro and in vivo biocompatibility testing of absorbable metal stents. *Macromolecular Symposia*, 2007. 253: p. 103-108.
- [11] H. Sigel and A. Sigel, Bioinorganic Chemistry of Metal toxicity, in *Metal ions in biological systems: concepts on metal ion toxicity*, 1986, CRC Press. p. 25.
- [12] G.S. Duffö and S.B. Farina, Corrosion behaviour of a dental alloy in some beverages and drinks. *Materials Chemistry and Physics*, 2009. 115(1): p. 235-238.
- [13] J.E. Moore Jr, J.S. Soares, and K.R. Rajagopal, Biodegradable stents: biomechanical modeling challenges and opportunities. *Cardiovascular Engineering and Technology*, 2010. 1(1): p. 52-65.
- [14] G.P. Talwar and L.M. Srivastava, Gastrointestinal tract, in *Textbook of Biochemistry and Human Biology*. 2003. p. 599-602
- [15] M. Mobin, M.A. Khan, and M. Parveen, Inhibition of mild steel corrosion in acidic medium using starch and surfactants additives. *Journal of Applied Polymer Science*, 2011. 121(3): p. 1558-1565.
- [16] E.S. Ferreira, C. Giacomelli, F.C. Giacomelli, A. Spinelli, Evaluation of the inhibitor effect of l-ascorbic acid on the corrosion of mild steel. *Materials Chemistry and Physics*, 2004. 83(1): p. 129-134.
- [17] M.S.S. Morad and A.A.A. Hermas, Influence of some amino acids and vitamin C on the anodic dissolution of tin in sodium chloride solution. *Journal of Chemical Technology & Biotechnology*, 2001. 76(4): p. 401-410.
- [18] A. Yamamoto and S. Hiromoto, Effect of inorganic salts, amino acids and proteins on the degradation of pure magnesium in vitro. *Materials Science and Engineering C*, 2009. 29(5): p. 1559-1568.
- [19] N.H. Helal and W.A. Badawy, Environmentally safe corrosion inhibition of Mg–Al–Zn alloy in chloride free neutral solutions by amino acids. *Electrochimica Acta*, 2011. 56(19): p. 6581-6587.
- [20] L. Ramalingam, L.B. Messer, and E.C. Reynolds, Adding casein phosphopeptide-amorphous calcium phosphate to sports drinks to eliminate in vitro erosion. *Pediatric Dentistry*, 2005. 27(1): p. 61-67.