BOSTON UNIVERSITY

THE EFFECT OF MAGNESIUM ON DENTINOGESIS OF HUMAN DENTAL PULP CELLS

Rania Salem[1,2], Chang Zhang [1], Dr. Sami Chogle [2], Dr. Laisheng Chou [1]

[1]Department of Restorative Sciences and Biomaterials, Boston University Henry M Goldman School of Dental Medicine
[2] Department of Endodontics, Boston University Henry M Goldman School of Dental Medicine

OVERVIEW

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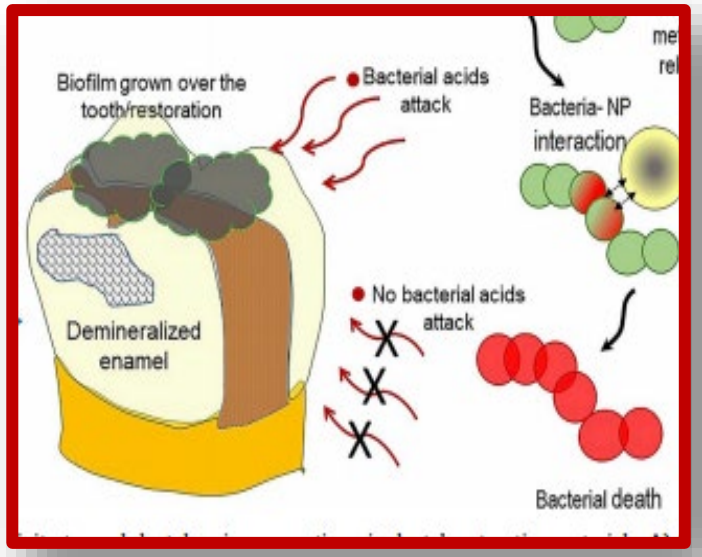
INTRODUCTION

- Dental caries is one of the most prevalent chronic diseases of all populations worldwide
- According to the report from the National Institute of Dental and Craniofacial Research (NIDCR) 92% of adults aged 20–64 years in the United States have had dental caries in their permanent teeth
- Over $ 66 billion is spent annually in the United States because of untreated dental caries

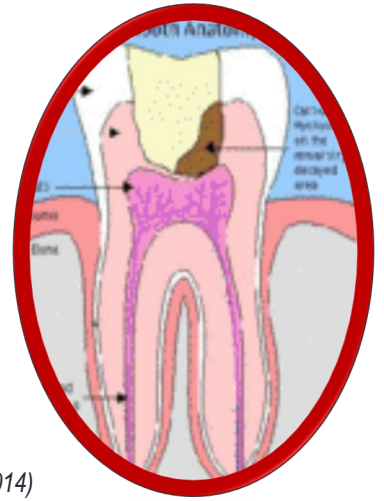
(*Selwitz et al., 2007*)
(Data from NIDCR Survey 2018)



- Dental pulp exposure from dental caries can cause pain and infection
- The currently available treatment scenarios in such condition are either root canal treatment if the pulp is irreversibly inflamed or pulp therapy if the pulp is still vital
- Vital pulp therapy aims to induce dentinal bridge formation to maintain pulp integrity and function

(*Renton &Wilson 2016)*
(Qureshi et al., 2014)

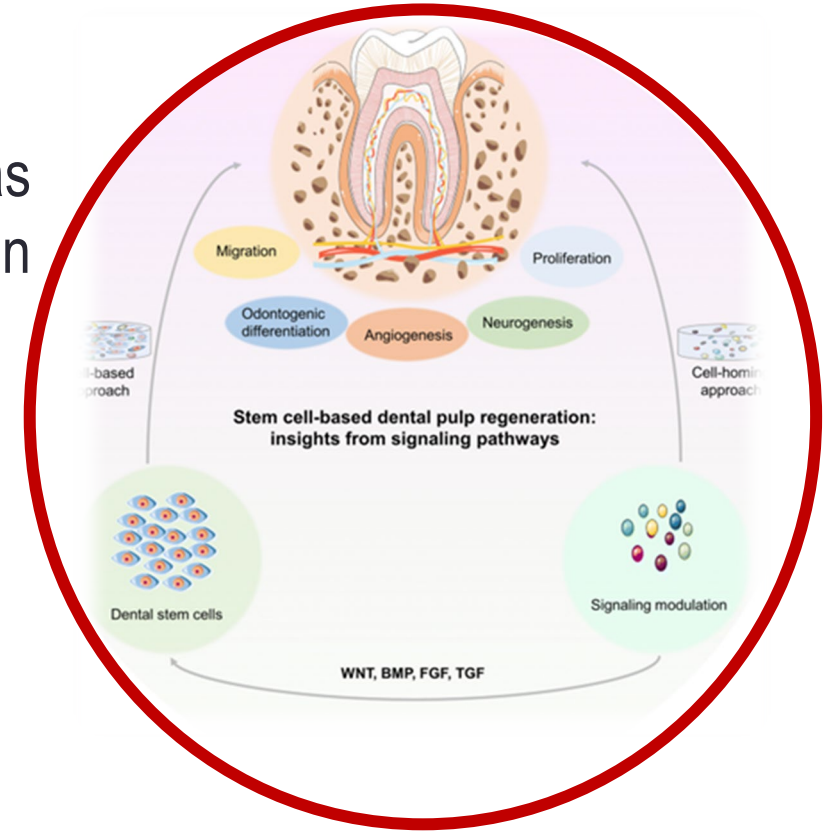
- Maintaining pulp vitality is a major challenge
- The development of pulp capping agents has been instrumental in promoting reparative dentin formation
- However, on-going research strategies have failed to overcome the limitations of existing pulp capping materials so that healthy and progressive regeneration of the injured tissues is attained

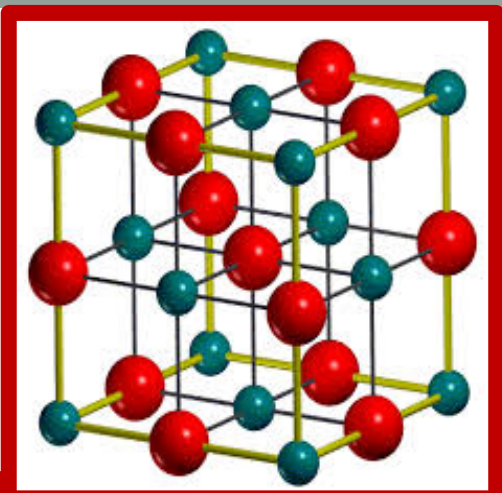


(Qureshi et al., 2014)

- Critical need exists to develop a novel therapy that induces dentinogenesis and remineralization similar to the natural process

- Introducing therapeutic ions into pulp capping materials has been considered as a new approach for enhancing regeneration of dental tissues.





Emerging evidence supports a notion that magnesium ions play indispensable bioactive roles

BACKGROUND

- Act as an intracellular second messenger
- Connect cell-surface receptor induction & cytosolic effectors
- Critical for ATP dependent phosphorylation of DNA,RNA & enzymes
- Modulation of signal transduction
- Affect energy metabolism
- Induce cell proliferation, differentiation & cell matrix interaction

(Hou.etal.,2020)
(Alhosani,M&. Leeny 2015)
(Wesmann et al., 1997)
(Saris et al., 2000)
(Serre et al.,1998)
(Staiger et al., 2006)

- Bone homeostasis
- Induce mineral metabolism
- Influence bone density & biomechanical property
- Associated in biomineralization of bone & teeth
- Cofactor for Alkaline phosphatase (ALP)
- Induction of osteoblast differentiation &increase in mineralization
- Increase in bone formation & cancellous bone volume

(Cashiglioni et al.,2013)
(Grober et al.,2015)
(Zhang et al.,2017)
(Wiesmann et al., 1997
Sans et al., 2000)
(Burmester et al .,2017
Wu et al .,2015,Kim et al
2017,Lin et al.,2019,
Terranora et al., 2016)
(Toba et al., 2000)

- Accelerate early osseointegration at titanium/bone interface
- Mg phosphate cements promote proliferation & differentiation of bone marrow stem cells
- Mg-doped glasses promote biocompatibility & enhance osteogenic bioactivity
- Porous magnesium scaffolds stimulate angiogenesis & induce new bone formation
- Mg- screws promote expression of BMP2 & VEGF in bone defects
- Mg- ceramics enhance differentiation & expression of osteoblast-related genes

(Galli et al., l2014,2015.2017)
(Sun et al .,2006 Hussain et al .,2002, Wei et al., 2016)
(Bob et, al .,2013)
(Sun. et,al,., 2006)
(Wang et al., 2017)
(Cheng .eta.,,2016)

- Evidence in the literature indicates that magnesium ions have a stimulatory effect on normal human osteoblasts

- Magnesium ions represent a promising strategy to replace damaged bone structures and restore their biological functions

- However, to date the effect of magnesium ions on dentin regeneration is intriguing largely unexplored

The mechanism behind magnesium relationship to human dental pulp cell behavior is not fully understood !!!!!!

- Because dentin closely resembles bone physically and chemically

Will magnesium ions have a similar mechanism of action on human dental pulp cells triggering regeneration of the injured/damaged dentin-pulp complex?

Research Questions

- 1- Will magnesium ions have a (stimulatory) biologic effect on human dental pulp cells (HDPCs) *in vitro* ?
- 2- Whether supplemental magnesium will affect such odontogenic activity enhancing or inhibiting proliferation, differentiation and biomineralization of human dental pulp cells *in vitro* ?
- 3- What will be the optimal concentration that can mostly induce such dentinogenic effect ?

Hypothesis

- Magnesium will have an inductive biologic effect on human dental pulp cells (HDPCs) *in vitro*

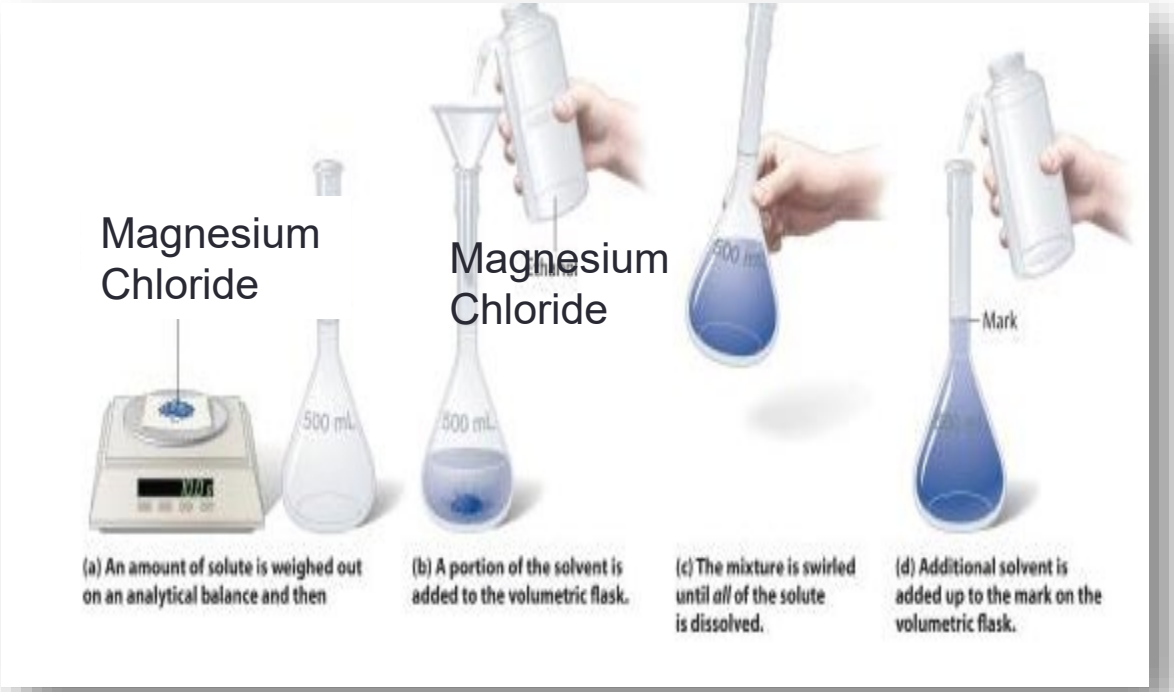
Research Objectives

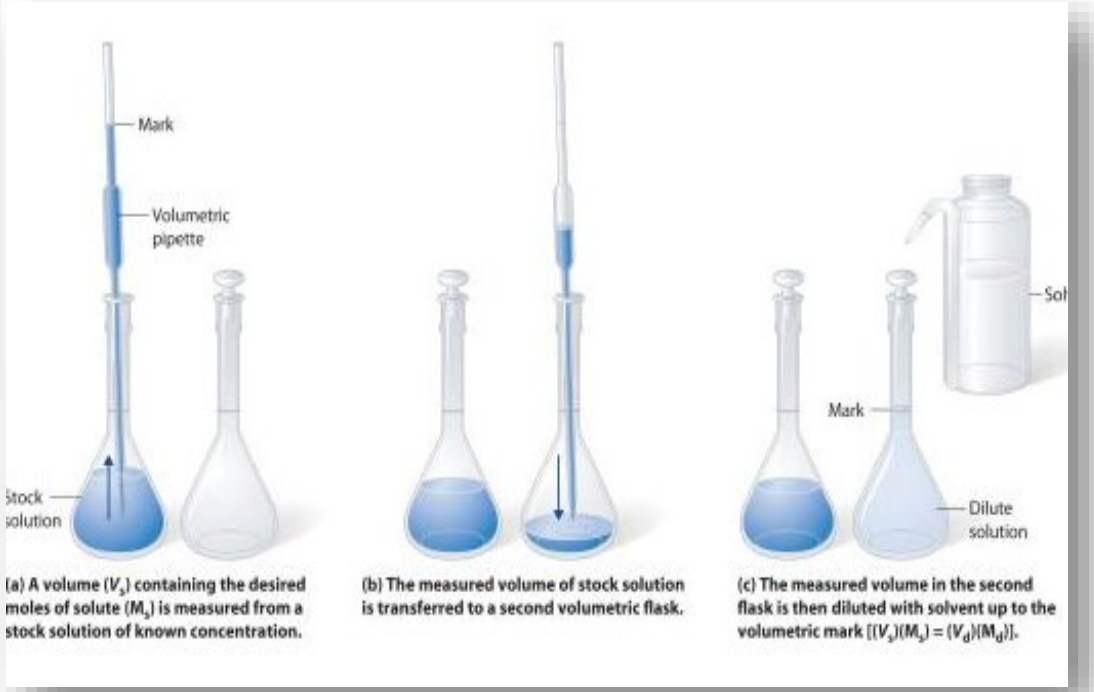
- 1- To prepare different concentrations of magnesium chloride

- 2- To assess the stimulatory effect of different concentrations of supplemental magnesium on attachment, proliferation, cell viability, and mineralization of human dental pulp cells (HDPCs) in vitro
- 3- To evaluate odontogenic differentiation by measuring
  - Alkaline phosphatase (ALP) activity
  - Dentin sialoprotein (DSP)
  - Dentin matrix protein-1(DMP-1)
  - Dentin sialo phosphoprotein (DSPP)

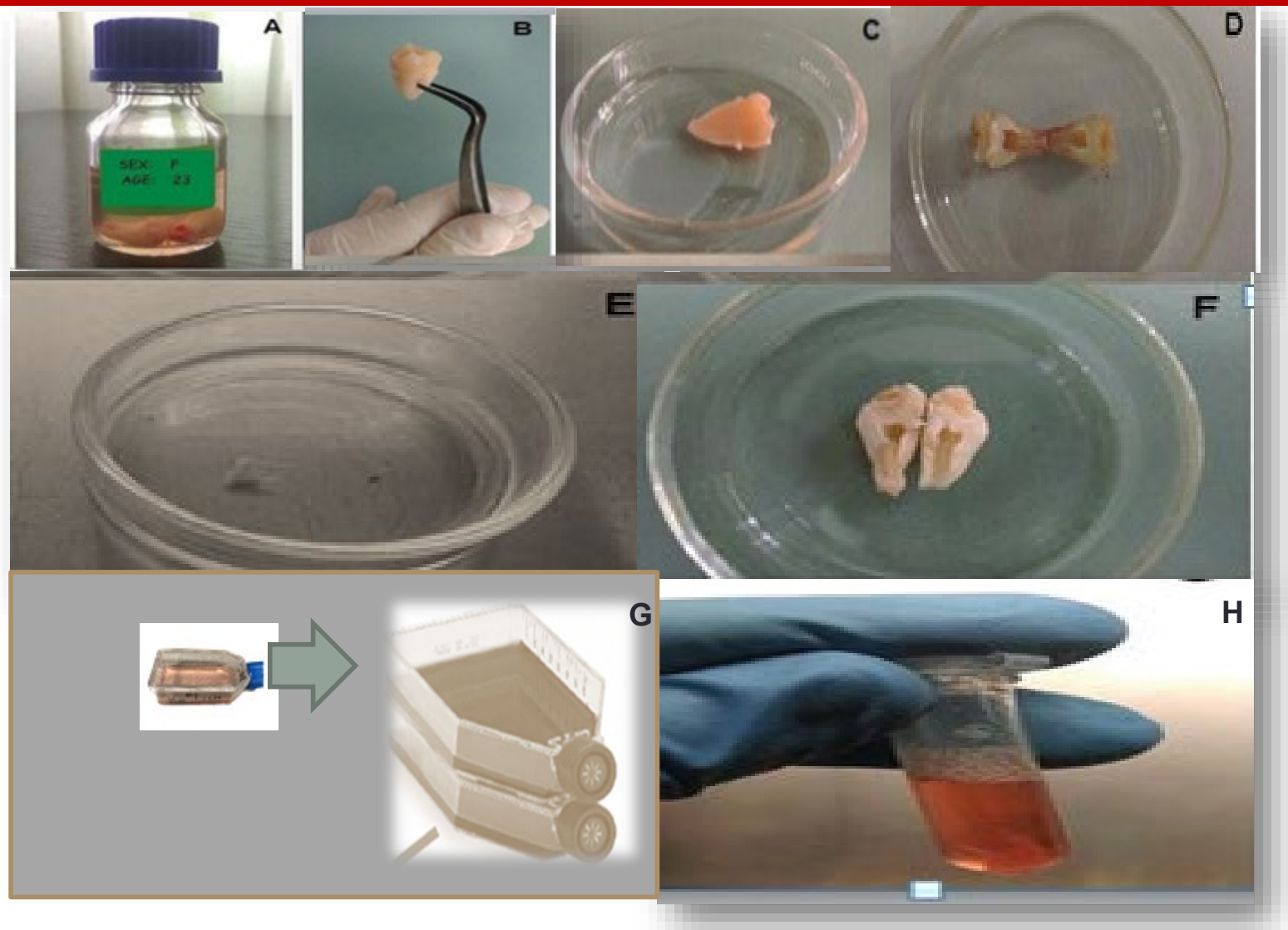
MATERIALS & METHODS

Preparation of Magnesium Chloride

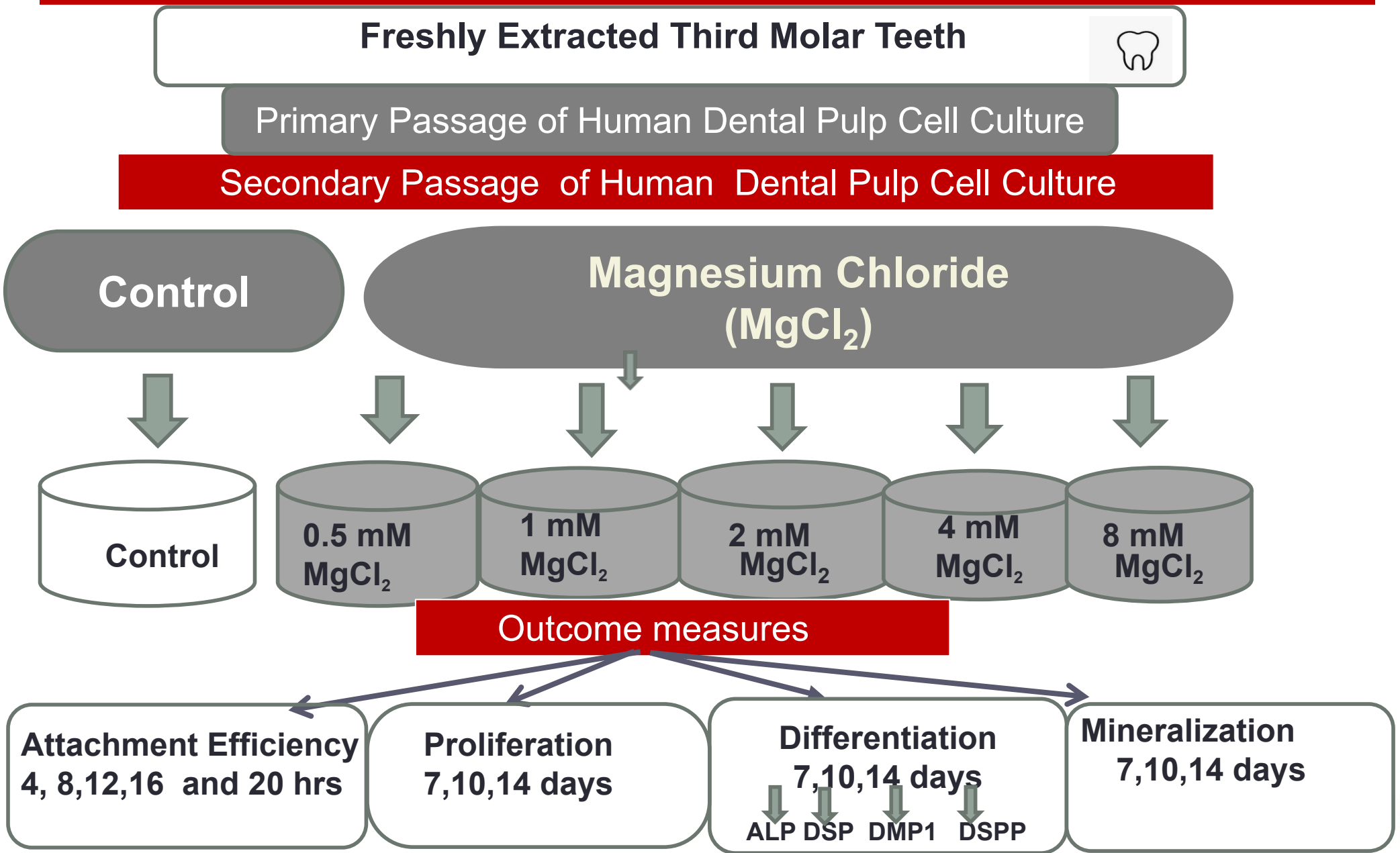




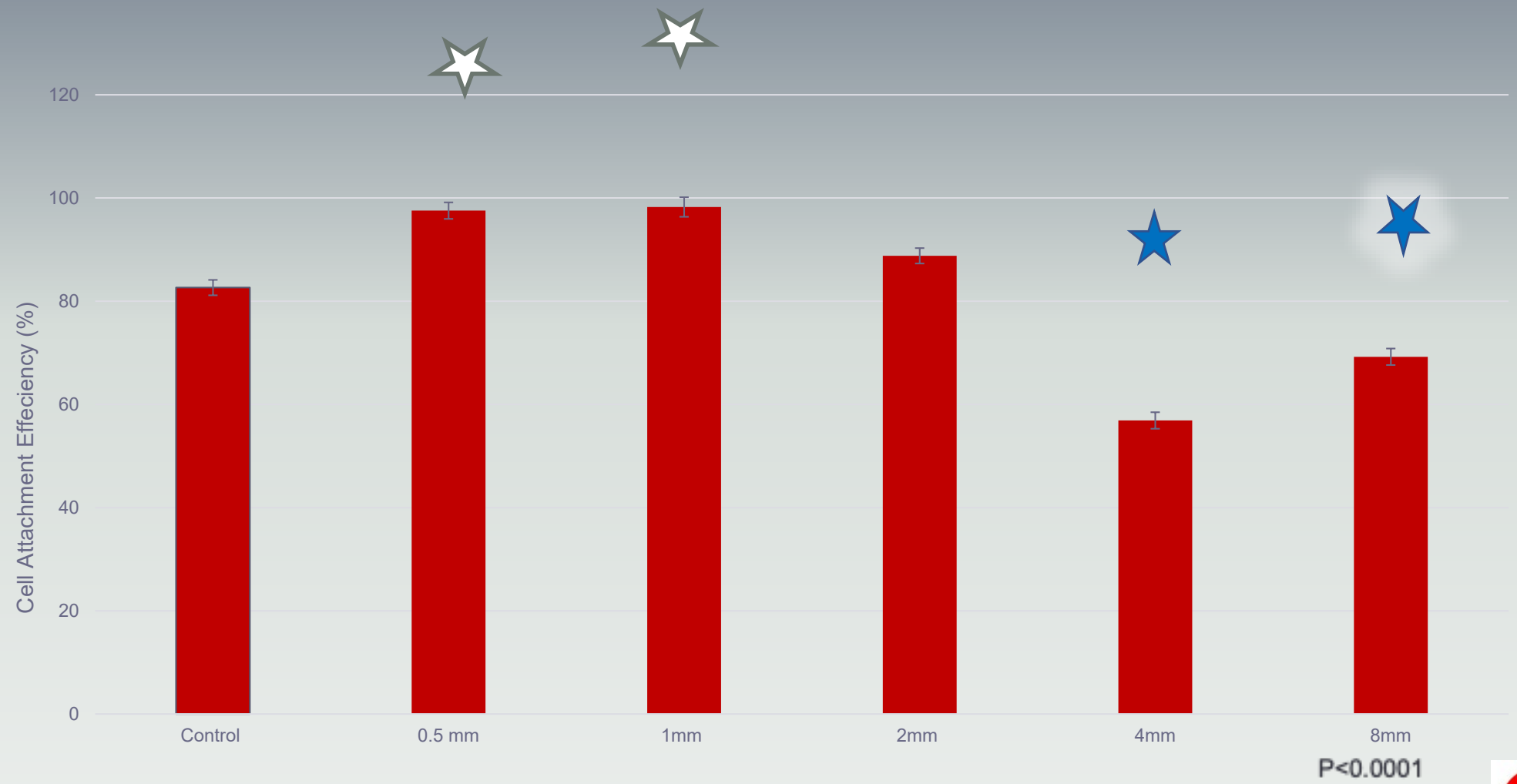
Steps of Human Dental Pulp Cells (HDPCS) Extraction



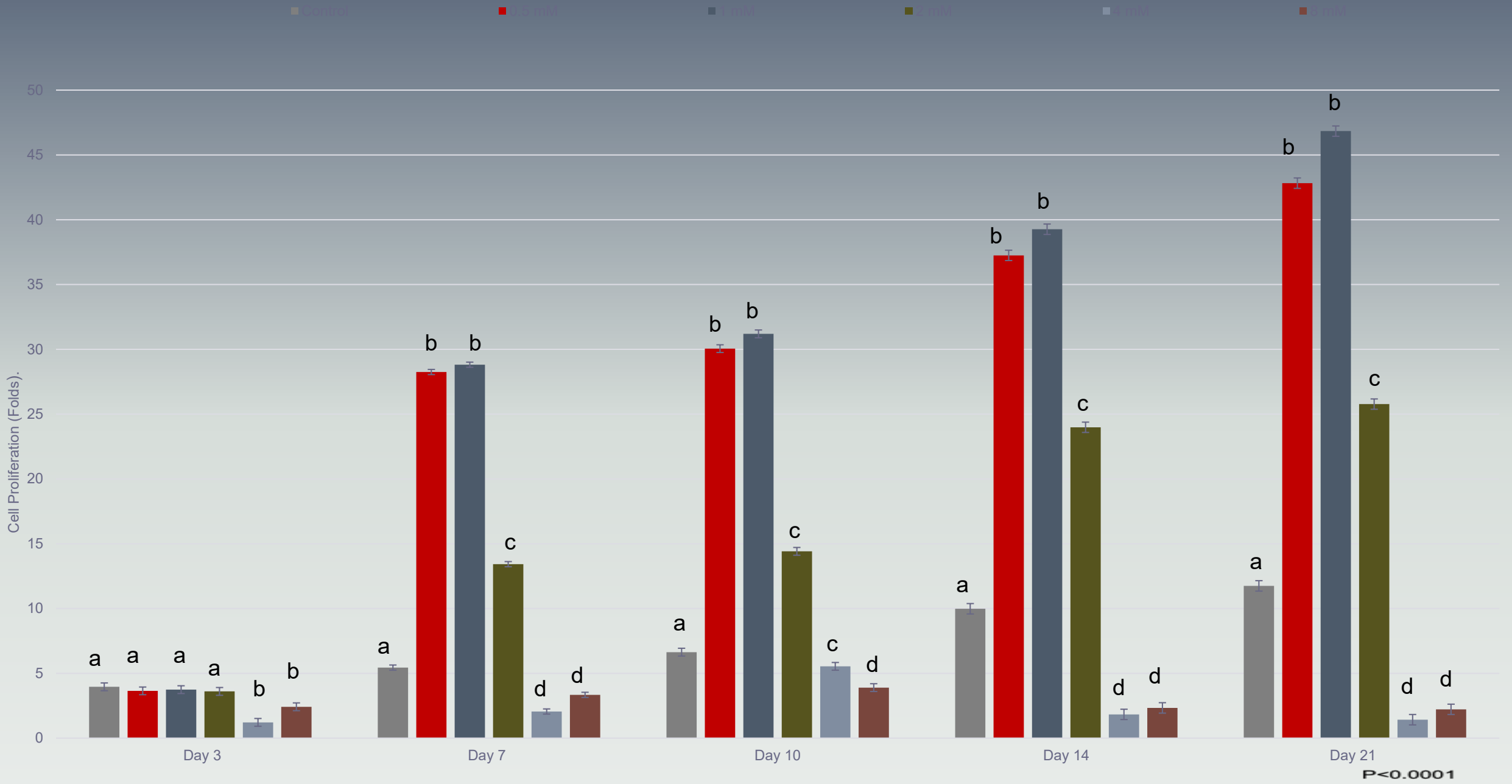
Human Dental Pulp Cells Cultured with Magnesium Chloride Concentrations



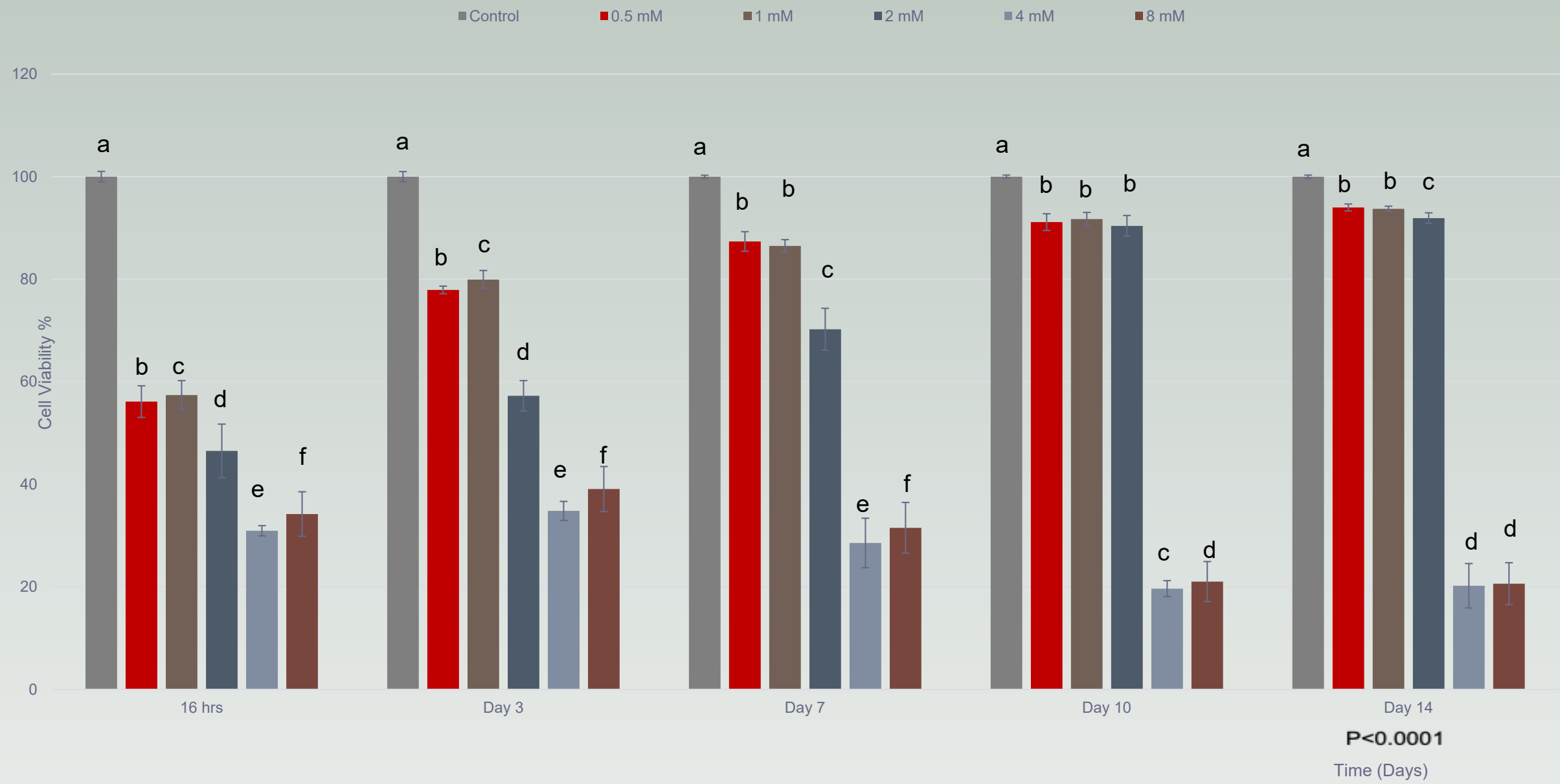
RESULTS



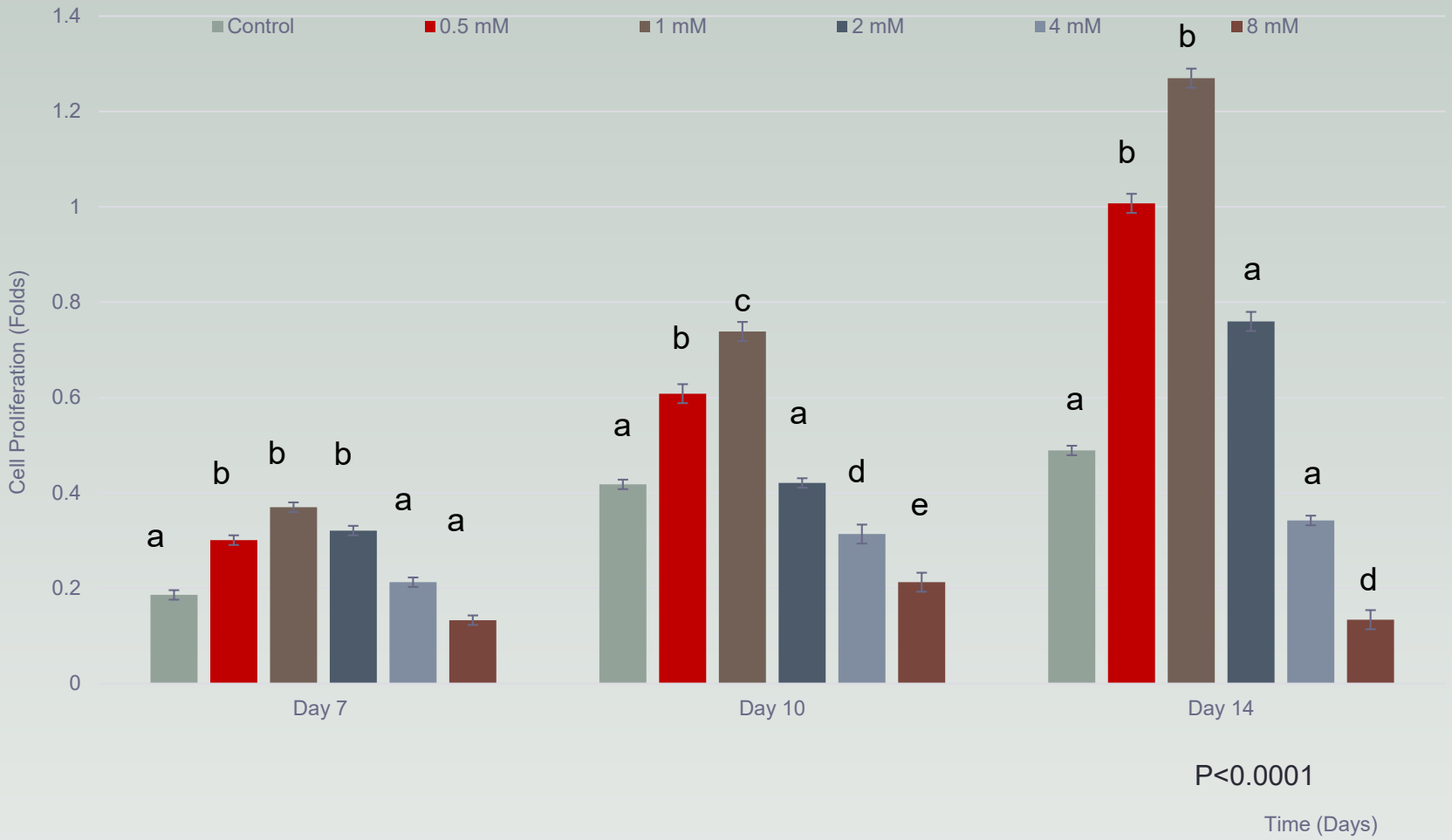
Histogram showing Cell Attachment Efficiency at 16 hours of all Magnesium Chloride ($MgCl_2$) Concentrations



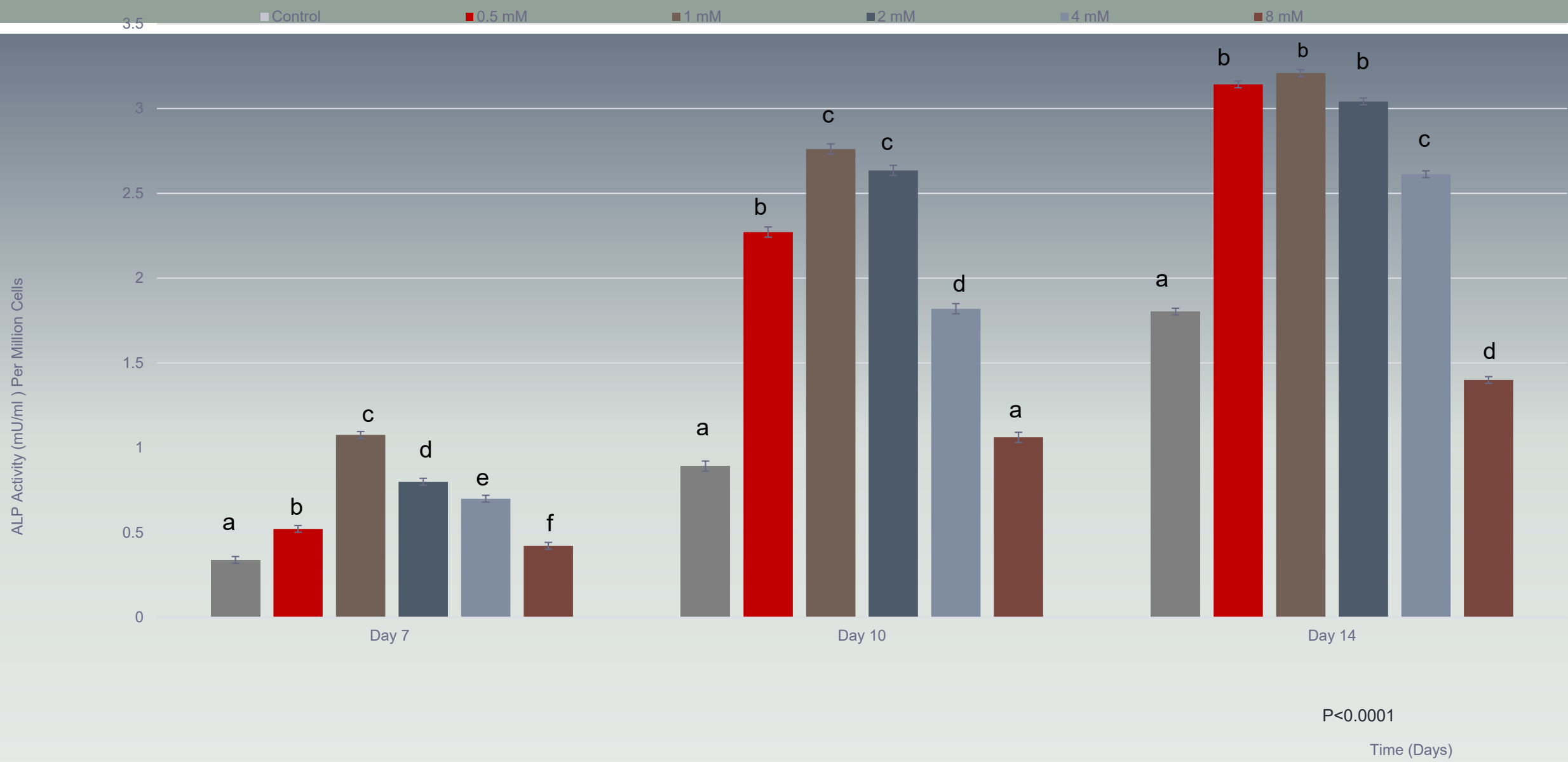
Histogram showing Cell Proliferation Rate of Magnesium Chloride ($MgCl_2$) at Different Time Intervals



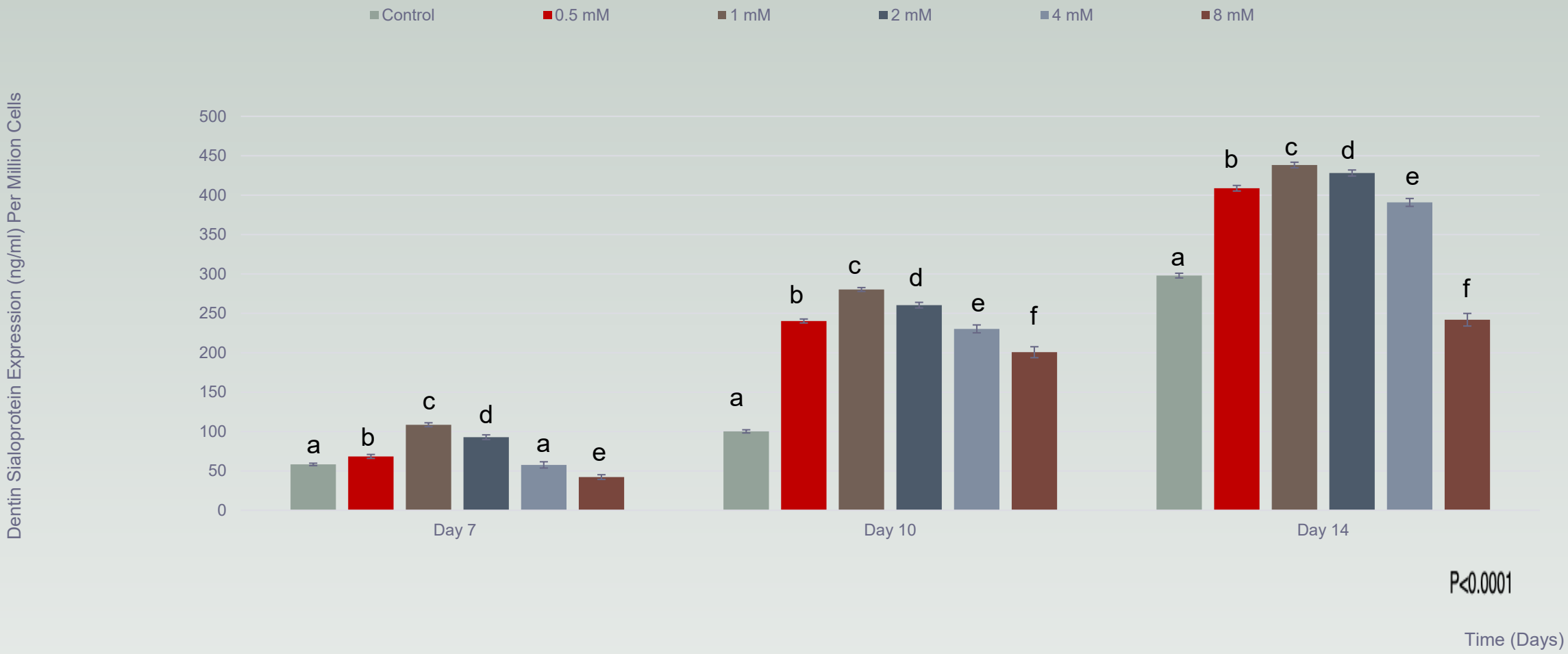
Histogram showing Cell Viability of Magnesium Chloride ($MgCl_2$) at Different Time Intervals



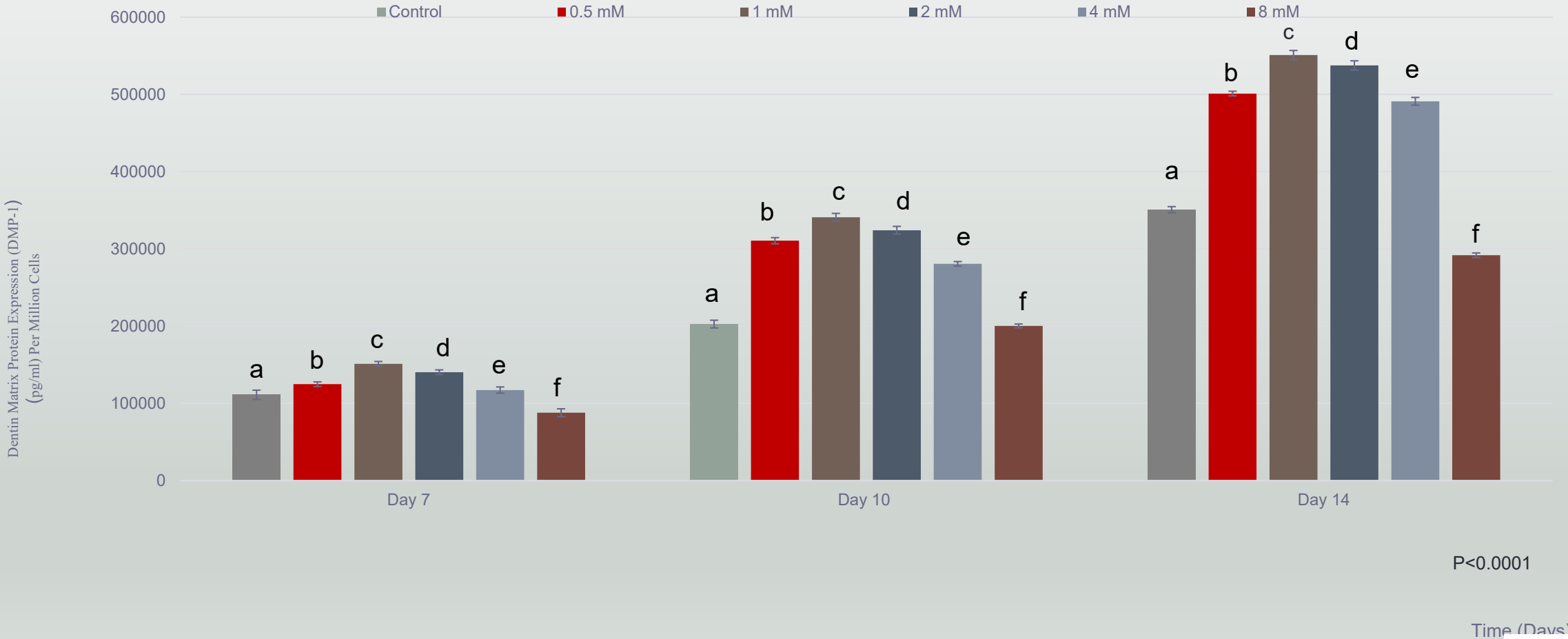
Histogram showing Cell Proliferation Rate of Magnesium Chloride ($MgCl_2$) at Different Time Intervals (Odontogenic Media)



Histogram showing Alkaline Phosphatase Activity of Magnesium Chloride ($MgCl_2$) at Different Time Intervals



Histogram showing Dentin Sialoprotein (DSP) Expression of Magnesium Chloride ($MgCl_2$) at Different Time Intervals

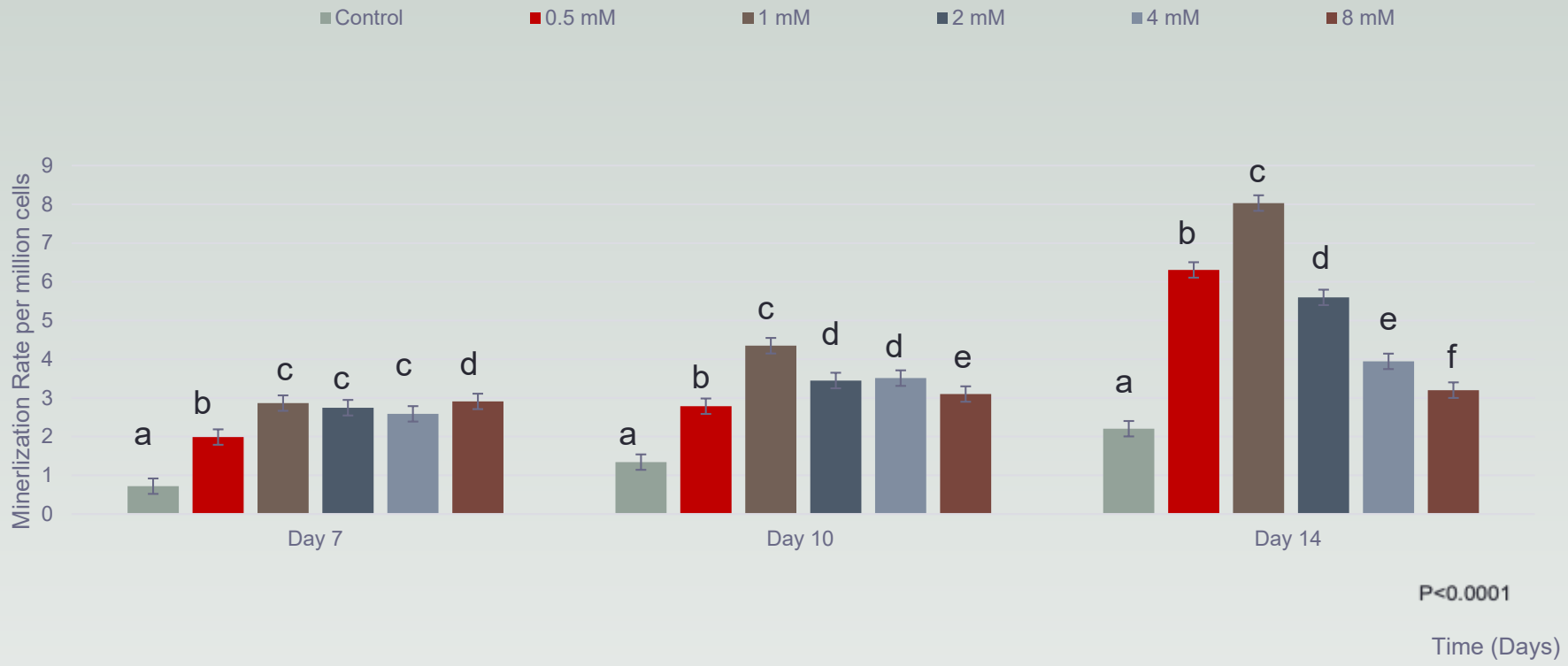


Histogram showing Dentin matrix protein1(DMP-1) Expression of Magnesium Chloride ($MgCl_2$) at Different Time Intervals

P<0.0001

Time (Days)

Histogram showing Dentin Sialophosphoprotein (DSPP) Expression of Magnesium Chloride ($MgCl_2$) at Different Time Intervals



Histogram showing Mineralization Rate of Magnesium Chloride ($MgCl_2$) at Different Time Intervals

CONCLUSIONS

Conclusions

- This is the first report to investigate the optimal magnesium concentration needed to induce human dental pulp cell attachment, proliferation, differentiation and mineralization

Conclusions

- This study showed that HDPCs with 0.5mM and 1 mM magnesium supplemental groups elicited the highest stimulatory effect on cell attachment efficiency, cell viability, proliferation rate, ALP activity, expression of odontogenic-related proteins (DSP, DMP-1, DSPP) and mineralization at all time points

Conclusions

- However, 8mM magnesium group had an inhibitory effect on HDPCS behavior showing lower ALP activity, expression of DSP, DMP-1, DSPP, and mineralization compared to the control

Clinical Considerations

- Future implementation of magnesium containing biomaterials show promise as a potential novel dental pulp capping material or additive in regenerative endodontics

Future Studies

- Further studies on the role of magnesium and its effect on odontogenic differentiation to determine the associated signaling pathway warrants closer examination

Acknowledgements

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Any
Questions
?

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