様　式　Ｃ－１９、Ｆ－１９－１、Ｚ－１９　（共通）

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研究課題名（和文）The combined application of mineral trioxide aggregate containing phosphorylated pullulan and colloidal platinum nanoparticles to control inflammation and facilitate dental pulp regeneration

研究課題名（英文）The combined application of mineral trioxide aggregate containing phosphorylated pullulan and colloidal platinum nanoparticles to control inflammation and facilitate dental pulp regeneration

研究代表者

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研究成果の概要（和文）：この研究は、歯科処置であるダイレクトキャッピング（DPC）におけるMTA（mineral trioxide aggregate)とリン酸化プルランの組み合わせ(MTAPPL)の可能性を評価しました。MTAPPLとCPNの使用が有望であることが示され、DPCの実行可能な代替手段としての可能性が示されました。CPNの治癒反応も良好であることが発見されました。これらの結果は、歯髄治療において新しい材料やアプローチを開発し、従来の材料の制限を克服することができることを示唆し、患者のアウトカムと生活の質の向上につながる可能性があります。

研究成果の学術的意義や社会的意義
Using CPNs and MTAPPL has significant impact in the dental field. The study develops new materials and approaches for dental pulp therapy, overcoming limitations of traditional materials and leading to better patient outcomes and quality of life.

研究成果の概要（英文）：The study aimed to evaluate the potential of a combination of mineral trioxide aggregate and phosphorylated pullulan for direct pulp capping (DPC), a dental procedure that involves placing a material directly on an exposed pulp to promote healing and prevent infection. We compared the effectiveness of the novel MTAPPL material to that of conventional MTA in inducing mineralized tissue formation and inflammatory pulpal responses. The results showed that MTAPPL exhibits comparable outcomes to MTA, indicating its potential as a viable alternative for DPC.

Additionally, the study investigated the healing response of colloidal platinum nanoparticles (CPNs) in exposed dental pulp. We found that the presence of endothelial cells, which are involved in angiogenesis, were present in the dental pulp after treatment with CPNs, indicating a favorable healing response. Overall, the study suggests that the combination of MTAPPL and CPNs hold promise for use in dental pulp therapy.

研究分野：Dentistry

キーワード：Direct pulp capping　MTA　CPNs　Pullulan

様　式　Ｃ－１９、Ｆ－１９－１、Ｚ－１９（共通）

１．研究開始当初の背景

Dental pulp repair is crucial for maintaining the health of teeth and gums. However, when the pulp tissue is damaged or inflamed, it can lead to the failure of dental pulp repair. The success of pulp tissue regeneration relies on a delicate balance between inflammation and regeneration, which requires the formation of new blood vessels through angiogenesis. Angiogenesis establishes the blood supply and brings oxygen, nutrition, and perivascular stem cells for regeneration.
Mineral trioxide aggregate (MTA) has been a popular and successful material used in vital pulp therapy, with an 85% clinical success rate. However, recent studies have shown that the combination of MTA and phosphorylated pullulan (MTAPPL) enhances its potential for hard tissue engineering. Phosphorylated pullulan has been found to work as a carrier for growth factors in hard tissue engineering, which makes it an excellent addition to MTA.
Colloidal platinum nanoparticles (CPN) are another material that has shown promise in the dental field. They have been found to improve resin-dentin bonding and act as an antibacterial agent. In a study conducted by Zhang et al., the bactericidal activity of CPN against Streptococcus Mutans was observed, indicating that CPN may be a candidate antibacterial agent for incorporation into dental restorative materials.
Based on the properties of CPN and MTAPPL, the combination of these materials may be an ideal material for dental pulp regeneration. The use of MTAPPL and CPN in dental pulp therapy represents a novel approach that could potentially overcome the limitations of conventional materials.

２．研究の目的

（1） To evaluate the healing process (angiogenesis) of rat dental pulps after direct pulp capping with the combined application of mineral trioxide aggregate containing phosphorylated pullulan (MTAPPL) and colloidal platinum nanoparticles (CPN).
（2） To evaluate the regenerative capability of rat dental pulps after direct pulp capping with the application of MTAPPL and CPN.
（3） To evaluate the characteristics of the combined materials in mineralized tissue formation.

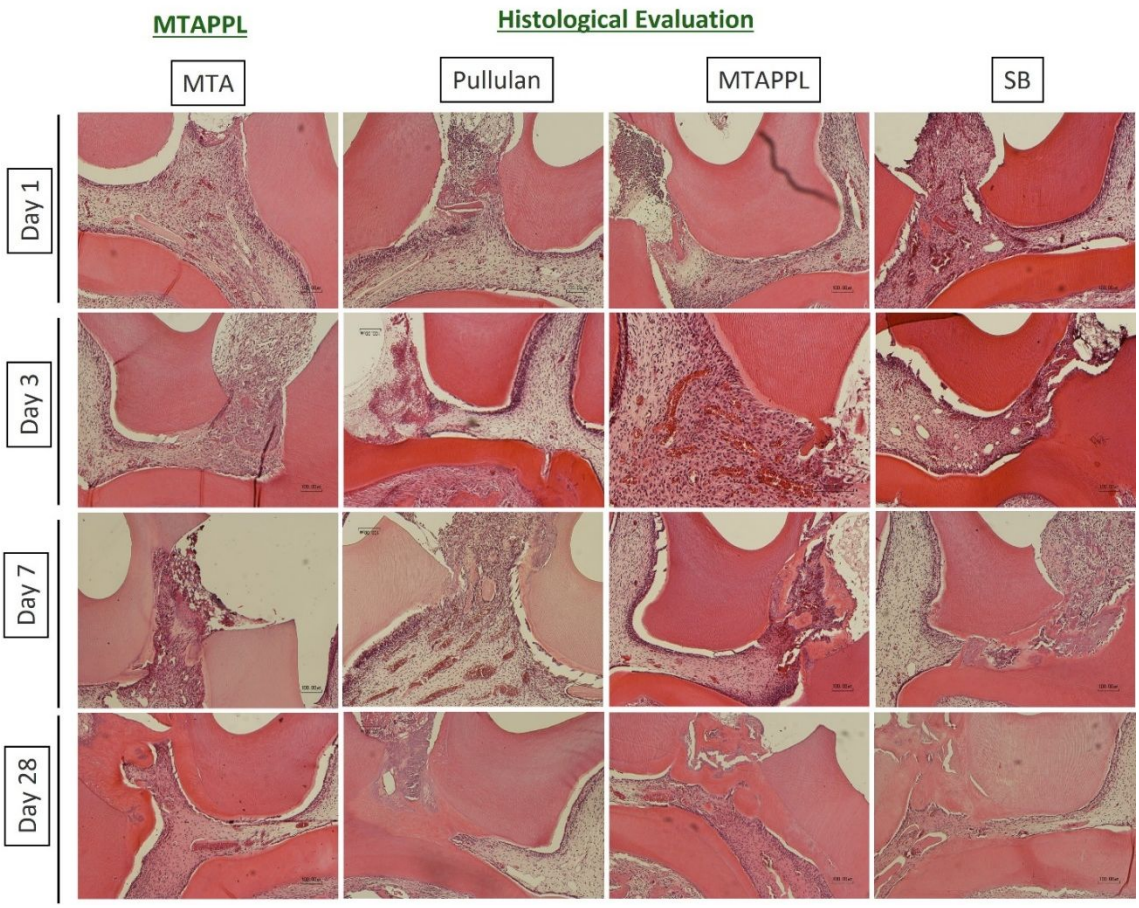
３．研究の方法

In this study, cavities were prepared in the maxillary first molars of male Wistar rats, and the dental pulps were intentionally exposed. The exposed dental pulps were then randomly divided into different groups based on the application of various materials, including MTAPPL, PPL, and different generations of colloidal platinum nanoparticles (1st generation PAA-PT, 2nd generation C-PT, and 3rd generation C-CYD), a conventional MTA (Nex-Cem MTA, NCMTA; positive control), and Super-Bond (SB; negative control). After the cavities were restored with SB, pulpal responses were observed at different time intervals (1-, 3-, 7-, and 28-day) using a histological scoring system. The statistical analysis was performed using Kruskal–Wallis and Mann–Whitney U-test with Bonferroni's correction, and the level of significance was set at 0.05. Finally, CD34 antigen was used to evaluate pulpal vascularization. The purpose of this experiment was to evaluate the effectiveness of various materials for dental pulp regeneration and to compare their performance with conventional materials such as MTA.

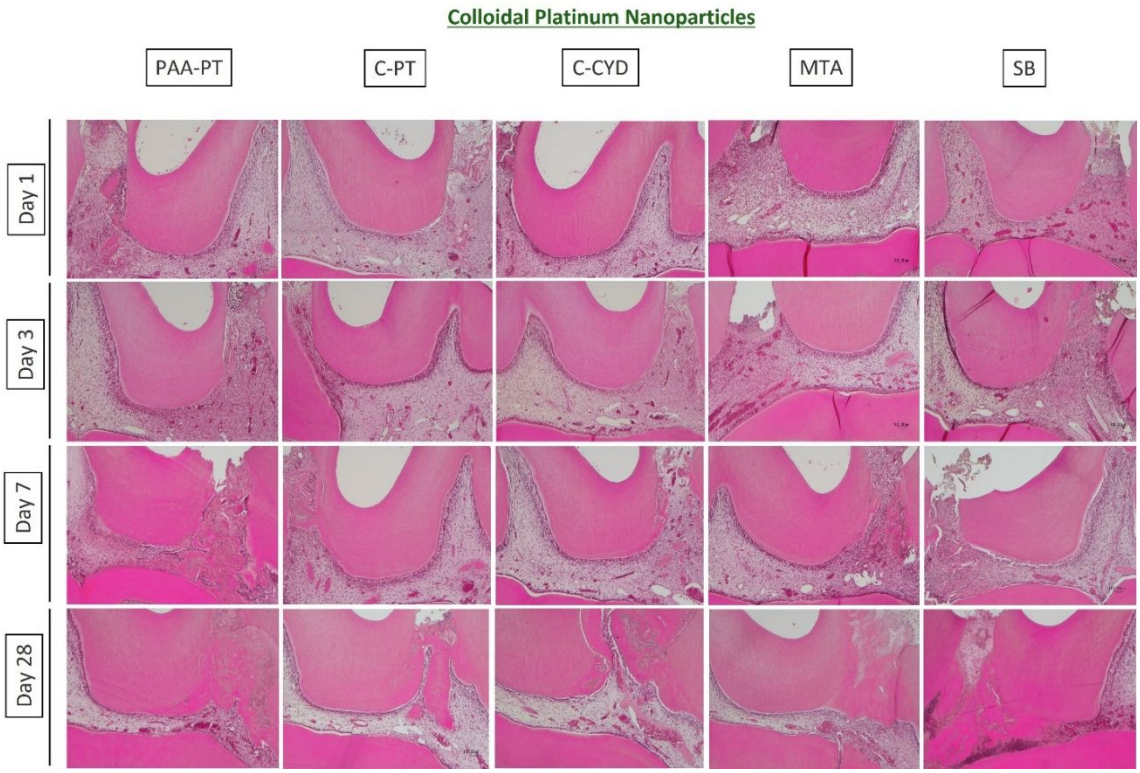
４．研究成果

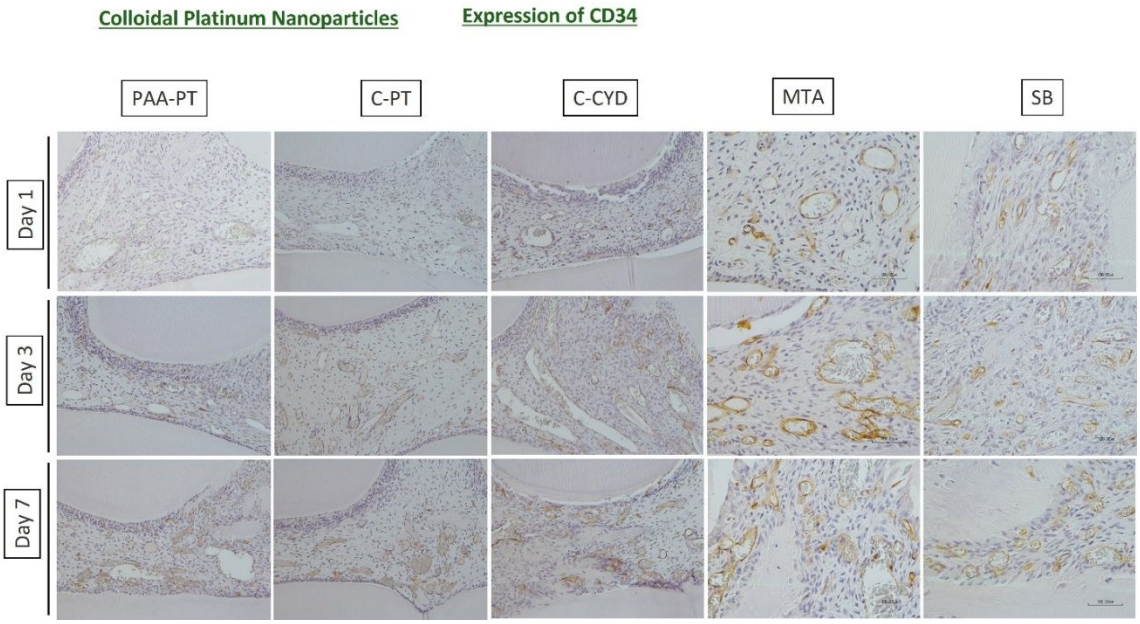
At day 1, there were mild inflammatory cells present in the MTAPPL and NCMTA groups, while PPL had fewer inflammatory cells. SB had a mild-to-moderate inflammatory response. A significant difference was noted between PPL and SB ($p < 0.05$), but no mineralized tissue deposition was observed. At day 3, moderate-to-severe inflammatory cells were present in

PPL and SB, while MTAPPL and NCMTA had a mild inflammatory response. Initial mineralized tissue deposition was observed in NCMTA, MTAPPL, and SB. A significant difference was observed between MTAPPL and PPL ($p < 0.05$). On day 7, all tested groups showed a thin layer of mineralized tissue with no or mild inflammatory response. At day 28, MTAPPL showed no inflammatory response, while NCMTA, PPL, and SB had mild inflammatory responses. Complete mineralized tissue barrier formation was observed in MTAPPL, NCMTA, and PPL with no significant difference ($p > 0.05$). SB exhibited incomplete mineralized tissue barriers, significantly different from NCMTA, MTAPPL, and PPL ($p < 0.05$). Positive staining with CD34 was noted in all groups on all observation days.



At day 1, no or mild inflammatory responses were observed in CPN group which was significantly less than the MTA and SB groups ($p < 0.05$). At day 3, numerous blood vessels were observed in the CPN group, which was significantly higher than the MTA and SB groups ($p < 0.05$). Mild inflammation was observed in the CPN group which was significantly less than the MTA and SB groups ($p < 0.05$). At day 7, no inflammation was observed in the CPN group which was significantly less than the SB group ($p < 0.05$). At day 28, CPT and CYD groups showed no inflammatory cell infiltration, whereas MTA and PAA-PT groups showed mild and SB groups showed moderate inflammatory cell infiltration. Significant differences were observed between SB groups with C-PT, C-CYD and MTA groups ($p < 0.05$). Complete mineralized tissue formation was observed in all the groups except the SB group which was significantly different ($p < 0.05$). All experimental groups showed positive expression of CD34 antigen. The development of well-defined micro-vessels were identified on endothelial cell surfaces from the marked expression of CD34 antigen. The expression of CD34 on the CPN group was significantly higher than the MTA and SB groups at day 1 and 3 ($p < 0.05$).





The study conducted on the combined application of MTAPPL for DPC and the use of CPNs in exposed dental pulp showed promising results. The novel MTAPPL exhibited comparable inflammatory pulpal responses and mineralized tissue formation inducibility to conventional MTA, indicating its potential for use in DPC. The favorable healing response of CPNs in exposed dental pulp, with the presence of CD34 endothelial cells indicating angiogenesis in the dental pulp, also highlights its potential for use in dental pulp therapy. These findings pave the way for further research and development of dental materials that can improve the success rates of vital pulp therapy procedures.

５．主な発表論文等

〔雑誌論文〕　計9件（うち査読付論文　0件／うち国際共著　0件／うちオープンアクセス　0件）

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２．論文標題 A novel method of 3D printing locating guide for abutment screw removal in cement-retained implant-supported prostheses	５．発行年 2022年
３．雑誌名 Journal of Dental Sciences	６．最初と最後の頁 -
掲載論文のDOI（デジタルオブジェクト識別子） 10.1016/j.jds.2022.02.017	査読の有無 無
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 －

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２．論文標題 Effectiveness of Direct Pulp Capping Bioactive Materials in Dentin Regeneration: A Systematic Review	５．発行年 2021年
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オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 －

１．著者名 TOIDA Yu、KAWANO Shimpei、ISLAM Rafiqul、JIALE Fu、CHOWDHURY AFM A、HOSHIKA Shuhei、SHIMADA Yasushi、TAGAMI Junji、YOSHIYAMA Masahiro、INOUE Satoshi、CARVALHO Ricardo M.、YOSHIDA Yasuhiro、SANO Hidehiko	４．巻 41
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掲載論文のDOI（デジタルオブジェクト識別子） 10.1016/j.jdsr.2023.02.002	査読の有無 無
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 －

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1．著者名 Islam Md Refat Readul、Islam Rafiqul、Ferdous Sultana、Watanabe Chiharu、Yamauti Monica、Alam Mohammad Khursheed、Sano Hidehiko	4．巻 10
2．論文標題 Teledentistry as an Effective Tool for the Communication Improvement between Dentists and Patients: An Overview	5．発行年 2022年
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1．著者名 Chen Fei、Wu Di、Islam Rafiqul、Toida Yu、Kawamoto Chiharu、Yamauti Monica、Sano Hidehiko	4．巻 15
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掲載論文のDOI（デジタルオブジェクト識別子） 10.3390/ma15124102	査読の有無 無
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 －

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3．学会等名 2022 IADR/APR General Session & Exhibition, China（国際学会）
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〔図書〕　計0件

〔産業財産権〕

〔その他〕

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6．研究組織

	氏名 （ローマ字氏名） （研究者番号）	所属研究機関・部局・職 （機関番号）	備考

7．科研費を使用して開催した国際研究集会

〔国際研究集会〕　計0件

8．本研究に関連して実施した国際共同研究の実施状況

共同研究相手国	相手方研究機関