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学位論文の題名	<p>Three-Dimensional Printing of an Apigenin-Loaded Mucoadhesive Film for Tailored Therapy to Oral Leukoplakia and the Chemopreventive Effect on a Rat Model of Oral Carcinogenesis (アピゲニン含有粘膜付着フィルムの3Dプリンタによる口腔白板症に対するオーダーメイド治療と口腔発がんモデルラットに対する化学的予防効果)</p> <p>Pharmaceutics, 14: 1575, 2022</p>
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Abstract: Oral leukoplakia, as a white lesion in the oral cavity, is precancerous in nature. Conservative treatment is preferable for this lesion, since surgical removal can markedly reduce the patient's quality of life. However, the long-term outcome of non-surgical treatment for the oral leukoplakia has been reported, that the cumulative 5-year cancer rate with oral leukoplakia is 1.2–14.5%, and the 10-year rate is 2.4–29.0%. In the present study, to find a more effective conservative treatment, we focused on the flavonoid apigenin and developed an apigenin-loaded mucoadhesive oral film using a three-dimensional (3D) bioprinter (semi-solid extrusion-type 3D printer). One of the advantages of this film is that the object can be designed in advance using a 3D computer-aided design (CAD), which allows for the on-demand manufacture of objects tailored to a specific individual. Apigenin-loaded printer inks are composed of pharmaceutical excipients (HPMC, CARBOPOL, and Poloxamer), water, and ethanol to dissolve apigenin, and the appropriate viscosity of printer ink after adjusting the ratios allowed for the successful 3D printing of the film. After drying the 3D-printed object, the resulting film was characterized. The chemopreventive effect of the apigenin-loaded film was evaluated using an experimental rat model that had been exposed to 4-nitroquinoline 1-oxide (4NQO) to induce an oral precancerous lesion. Treatment with the apigenin-loaded film showed a remarkable chemopreventive effect based on histological and immunohistological analyses of the specimens. These results suggest that the apigenin-loaded mucoadhesive film may help prevent carcinogenesis. In addition, it is possible to form the dosage according to the individual oral cavity shape based on the patient's image data, and to adjust amount of drug content by this 3D printer, therefore it is thought that this film could become a completely new topical agent.