Phosphoryl oligosaccharides of calcium (POs-Ca®)

TOMOKO Tanaka

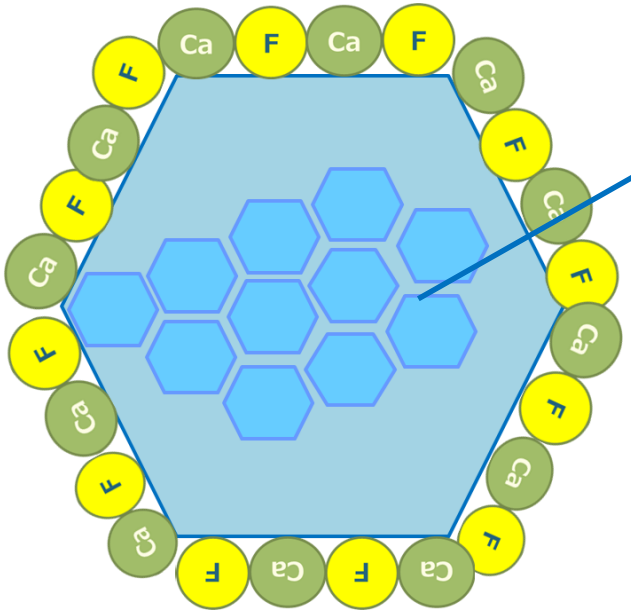
Institute of Health Sciences
Ezaki Glico Co., Ltd.

Cavity and Periodontal disease can be effectively prevented and controlled by the practice of self care, community care and professional care.
(WHO 1994)

World Health Organization

High concentration Treatment

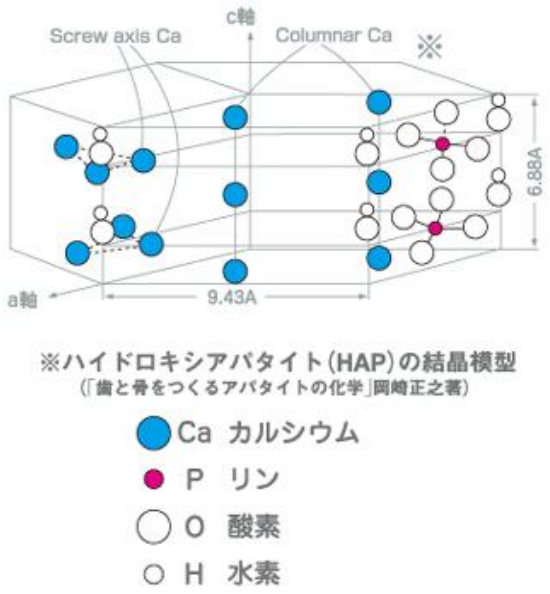
Coating effect by CaF_2



$$Ca_{10}(PO_4)_6(OH)_2+20F^-+8\,H^+ \rightarrow 10CaF_2+6\,HPO_4^{2-}+2H_2O$$

Low concentration Treatment

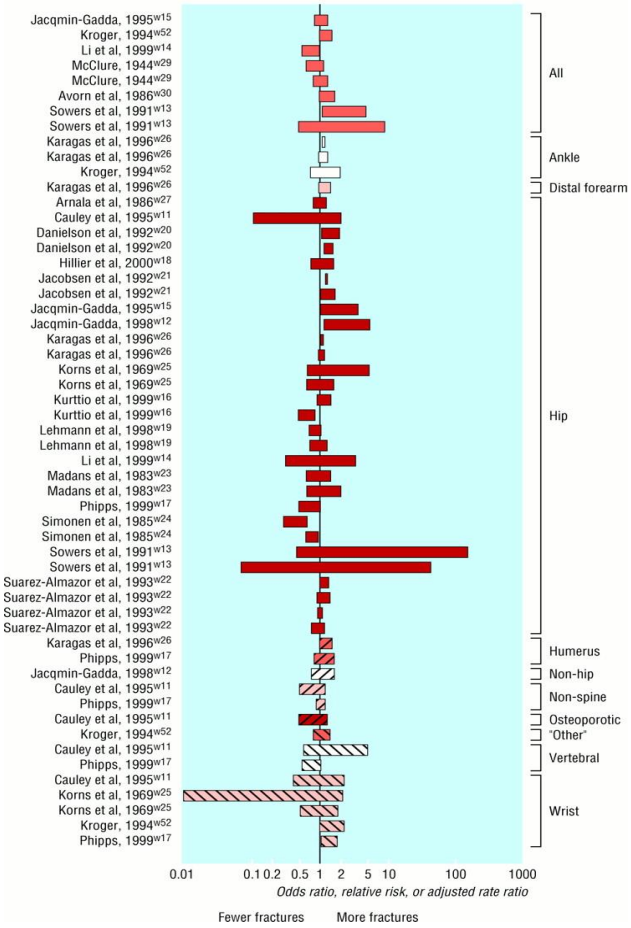
Quality improvement by FAp formation

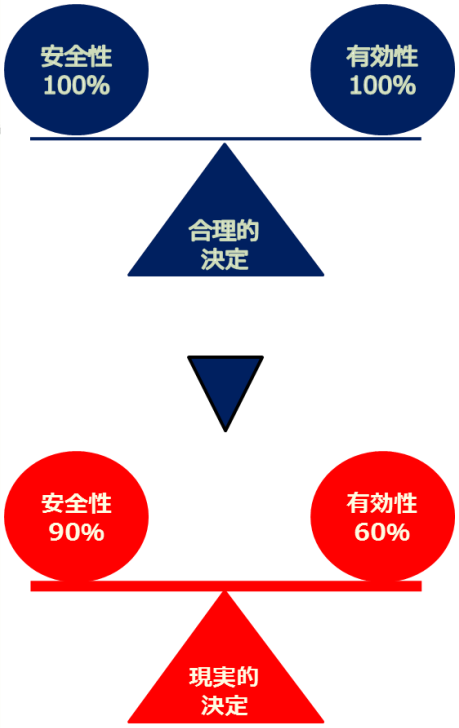


$$Ca_{10}(PO_4)_6(OH)_2+2F^- \rightarrow Ca_{10}(PO_4)_6F_2+2\,OH^-$$

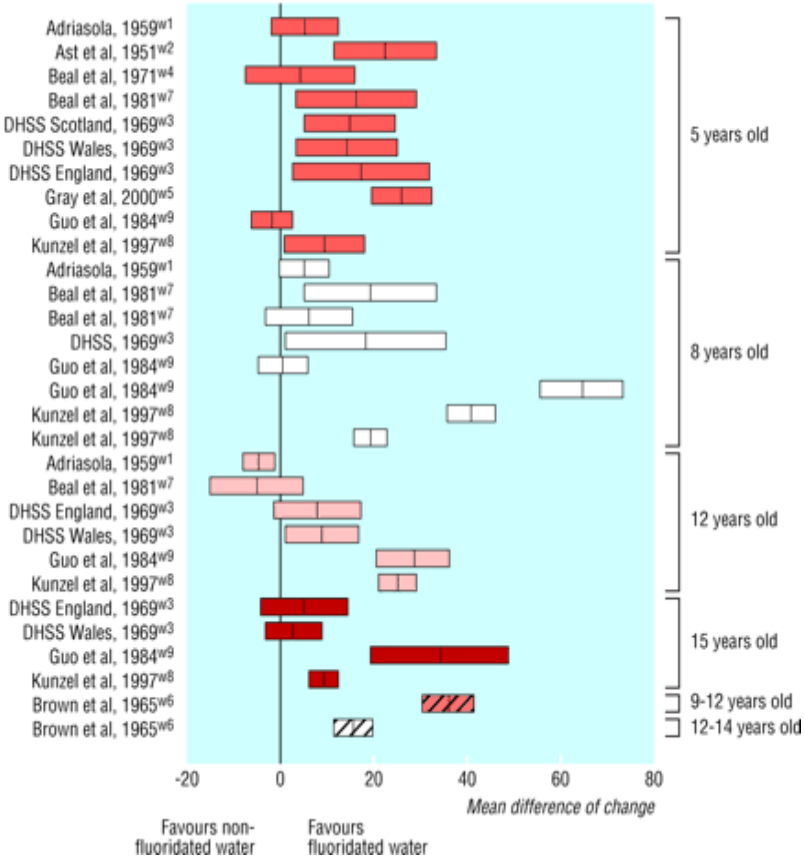
Safety of fluoride

安全性





有効性



Systematic review of water fluoridation
BMJ 2000; 321 :855

The concentration of Water Fluoridation (WF) was set 1.0 ppm fluoride
It was based on the review, safety 90% effect 60%

Method and concentration of Fluoride

method		Fluoride Type	Concentration	Inhibition rate
Systemic application  	Tap water	NaF KF	0.6～1.0 ppm	40～60% (Adult) 30% (Child)
	Food	NaF	200mg/kg food	20～50%
	Medicine	NaF	0.5 ～1.0 mg/day	20～40%
Topical application 	Tooth surface application	NaF SnF_2	300～19400 ppm	20～50%
	Mouthwash	NaF	226ppm/day 900ppm/week	20～50%
	Toothpaste	Ma_2PO_3F NaF SnF_2	1000~1500 ppm	15～20%

おいしさと健康
Glico

POs-Ca for oral care

Technical problems

① **Calcium solubility** in saliva (neutral)

Calcium solubility is very low in saliva

☞ Develop new material (calcium) = **POs-Ca** (high solubility)

② **Crystallinity of calcium that penetrate in the tooth**

The calcium penetrating in tooth is not always tooth crystals.

☞ Development the method of tooth crystal

☞ Clinical study (Chewing gum product POs-Ca containing)

③ **Solubility of calcium with fluoride**

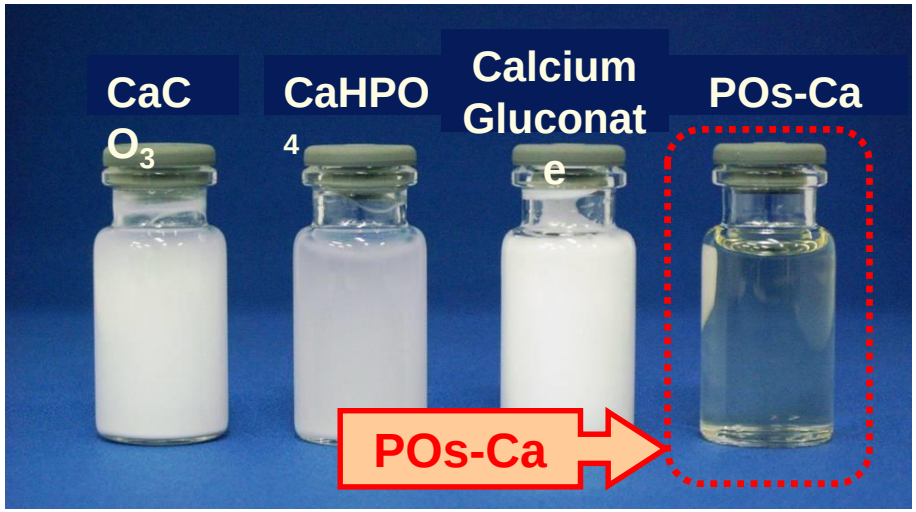
Fluoride has high reactivity, the solubility of fluoride with calcium is very poor.

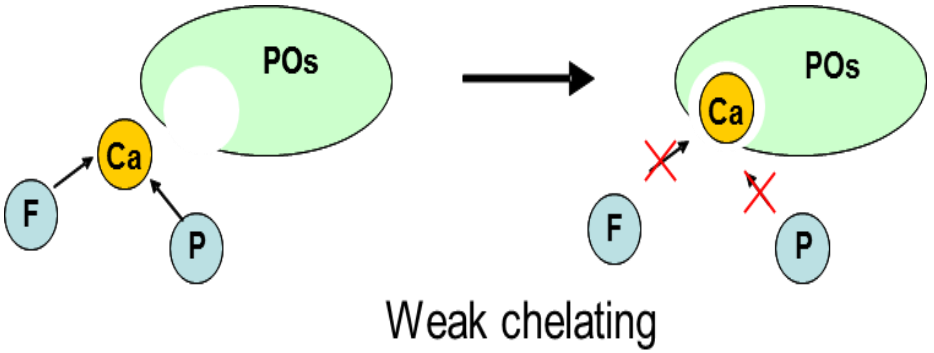
☞ Improve solubility of fluoride with calcium by using POs-Ca

☞ Demonstrated improvement of tooth hardness by improving fluoride penetration

① POs-Ca （highly soluble in water）

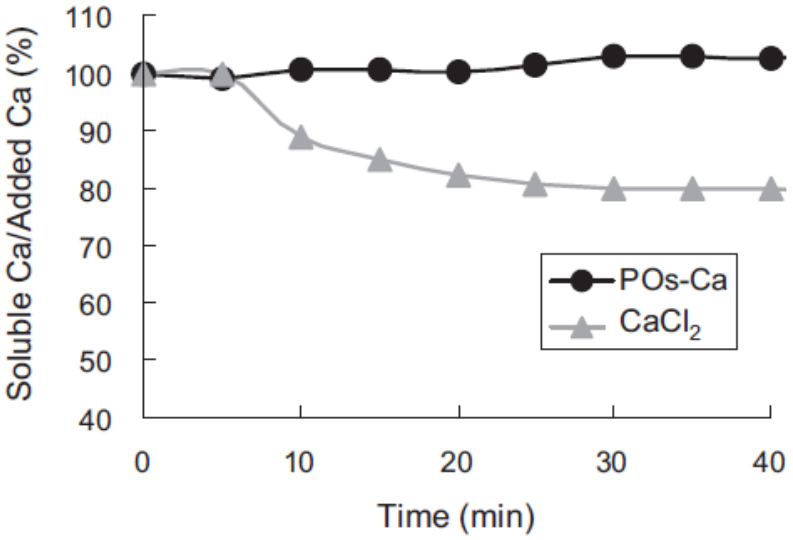
Calcium salts for food with the same calcium content added in water

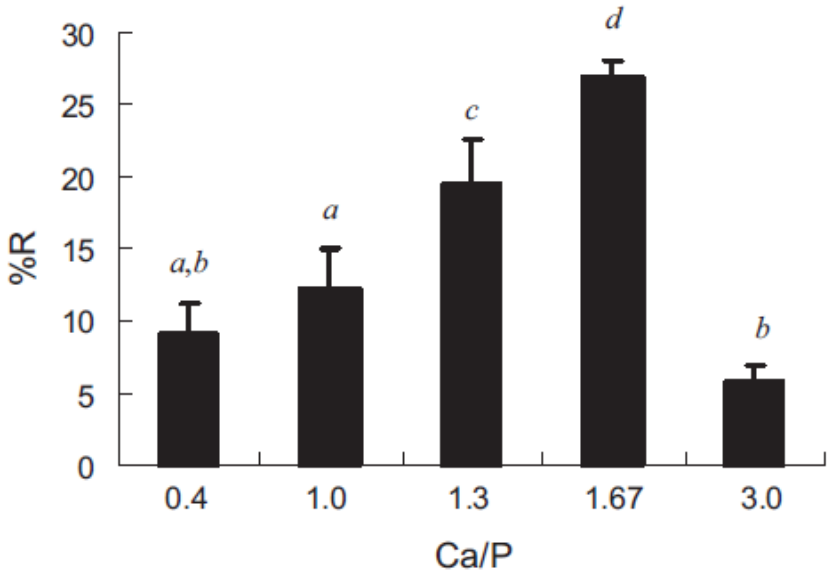




Mild chelating of calcium by phosphate residue stabilize calcium ions in saliva

② Ca/P = 1.67 is the best ratio for remineralization



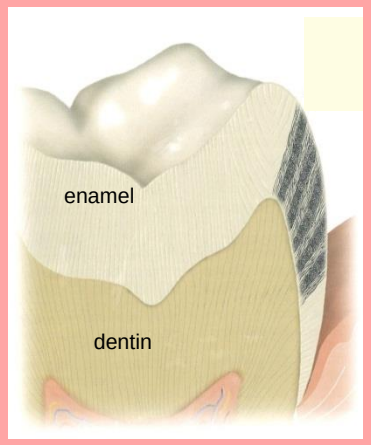


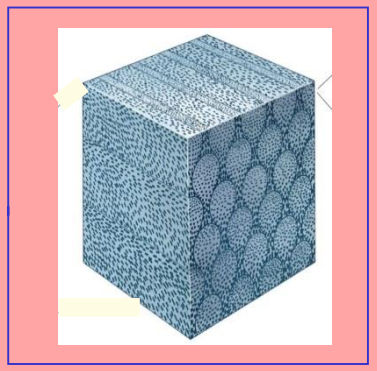
Stability in saliva
POs-Ca > $CaCl_2$

Ca/P=1.67 is the best, which is the same as that of hydroxyapatite.

***Arch. Oral Biol* (2013)**

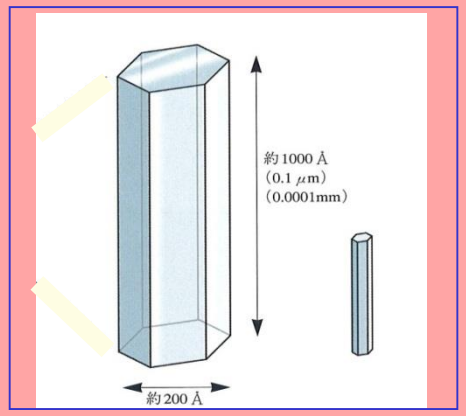
Change saliva as liquid enamel by using POs-Ca

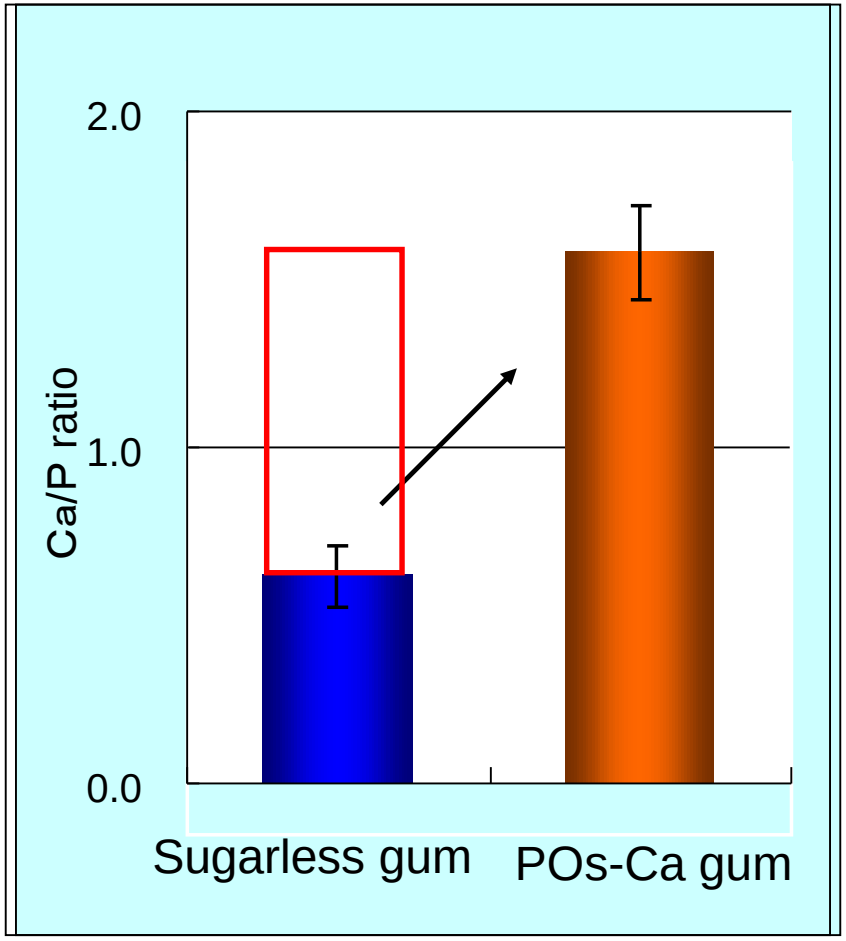




Ca/P ratio
1.67

HAp crystal

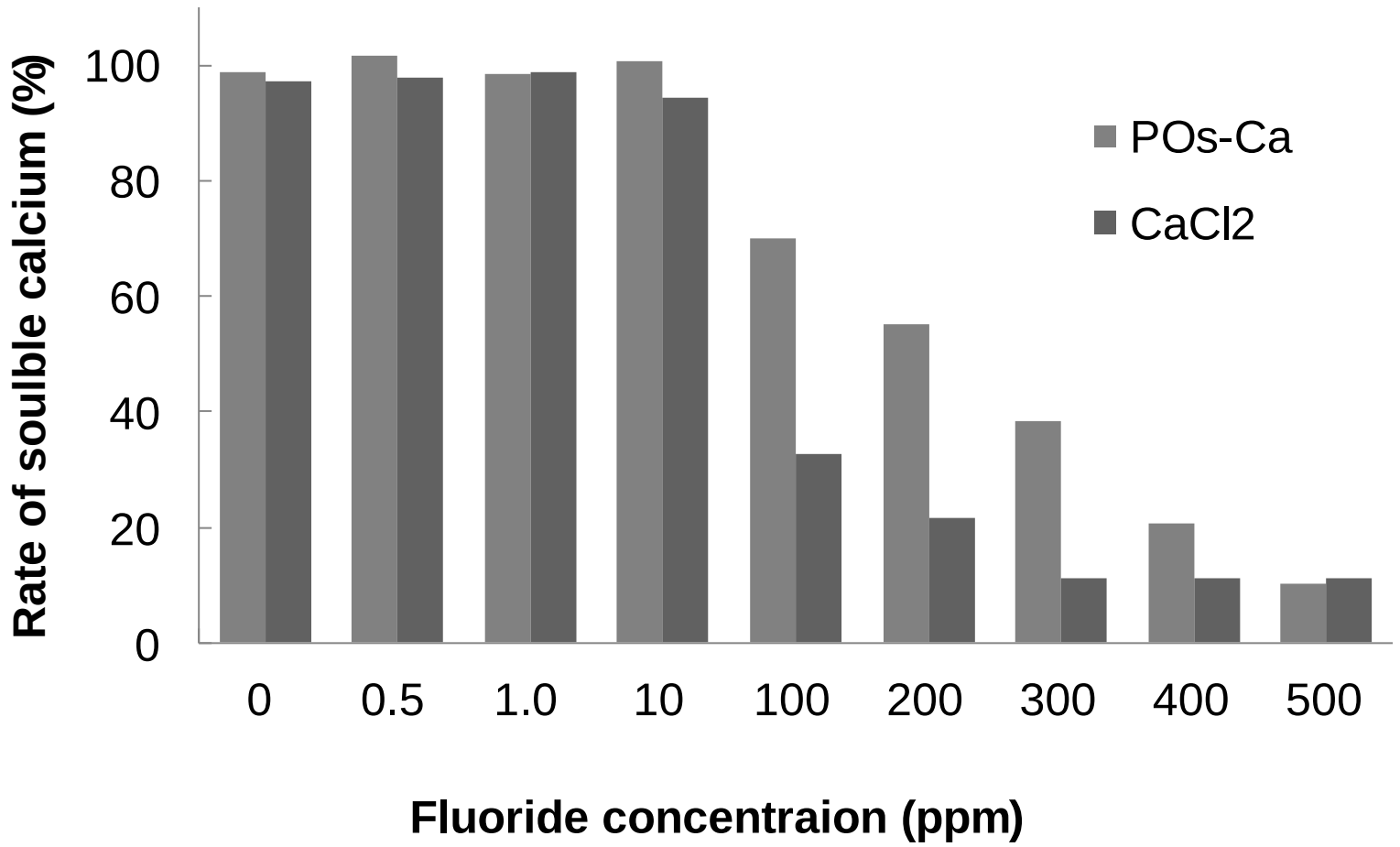




Ca / P concentration ratio of chewing gum for 10 minutes

Saliva Ca/P ration = 1.67

③ Solubility of calcium under various fluoride concentrations

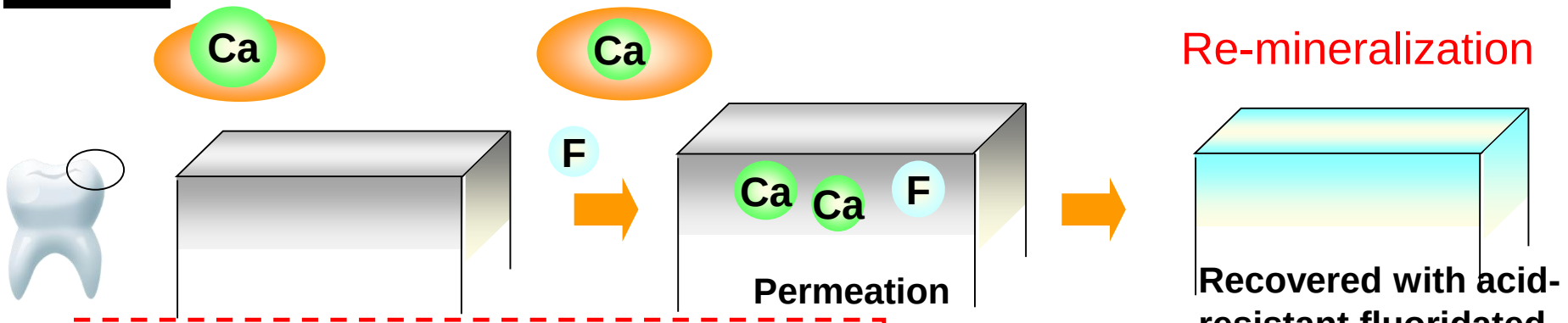


③ Re-mineralization effect of POs-Ca

POs-Ca is new calcium which **dissolves in saliva.**

→ Dissolved POs-Ca penetrates into tooth to cure early-stage caries.

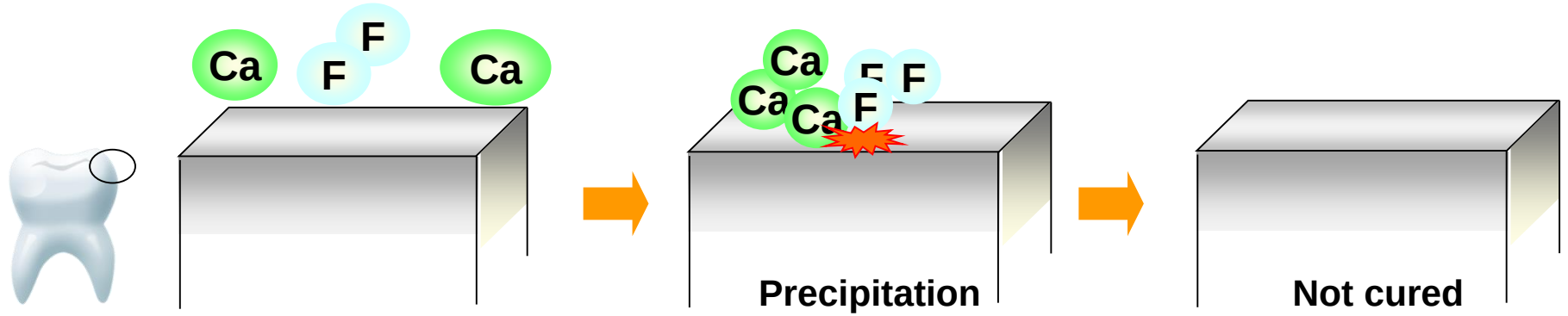
POs-Ca



Ca ion from POs-Ca can be dissolving with fluoride ion in saliva.

Don't bond with fluoride and not complex with Ca-F.

Conventional calcium



For anti caries

Clinical study

■機能性ガムの食生活への介入効果

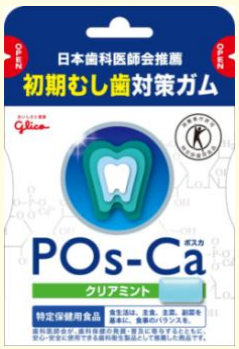
Healthy teeth

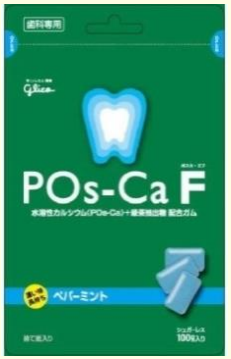
Dissolution of calcium ⇩⇧ Restoration of calcium

Early-stage caries

Ca

F





Without daily care ⇩

Cavity

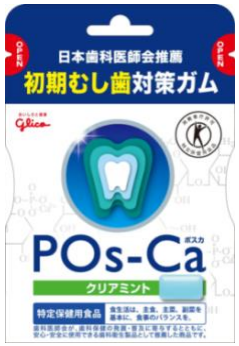
⇩

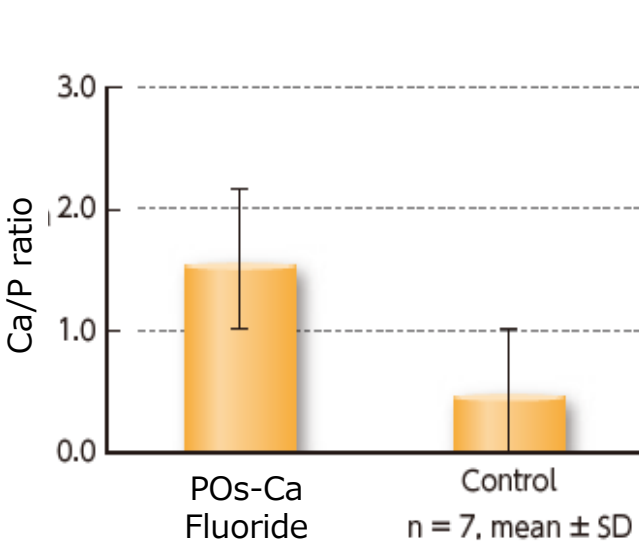
Not curable without dental treatment

Keep the quality of life, Effortless

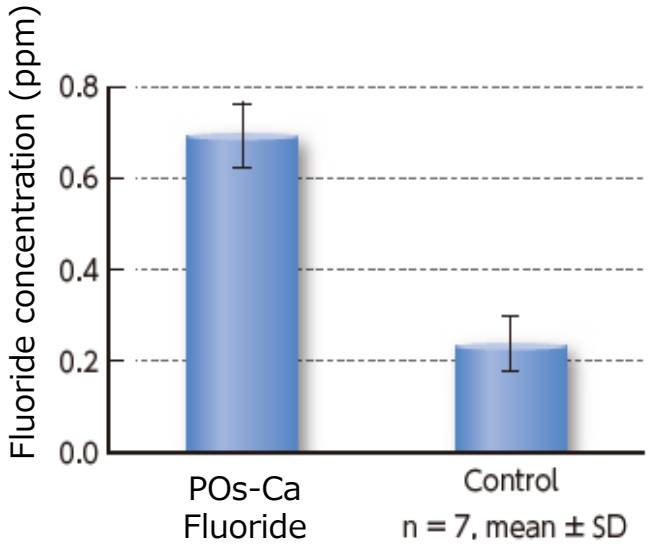
Bioavailable calcium and fluoride ions in saliva

Expediting remineralization and recrystallization and strengthening of enamel by calcium and fluorides ions





Golden ratio 1.67



Same environment → Water fluoridation

Ca from POs-Ca + **F**luoride from tea extract

Clinical trial for chewing gum“POs-Ca”

Subject

The study was conducted by Tokyo Medical Dental University.

- Healthy students at a university (n=36, over the age of 20)
- Dividing into 3 groups, taken one of 3 chewing gums, in each period.

Samples

Sugar-free chewing gums with

- No calcium **(Control)**
- 2.5% POs-Ca **(POs-Ca)**
- 2.5% POs-Ca and 1.2% green tea extract (fluoride source, 1000 ppm F) **(POs-Ca+F)**

period	2 w	1 w	2 w	1 w	2 w
Group A	Gum α		Gum β		Gum γ
Group B	Gum β	Washout	Gum γ	Washout	Gum α
Group C	Gum γ		Gum α		Gum β

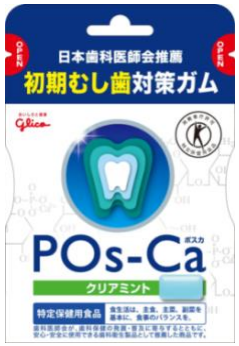
Ingestion protocol of the gum samples

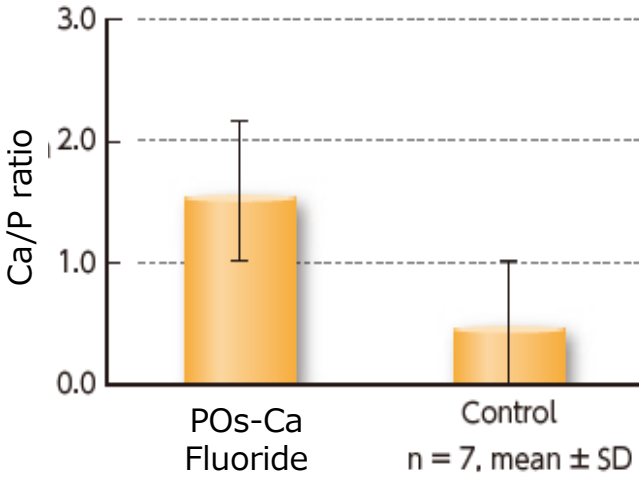
- Wearing the oral appliance for 20 min during gum chewing, for 20 min after gum chewing,
- 3 times a day / 2 pellets,
- 20 minutes chewing, for 14 days.

Oral appliance

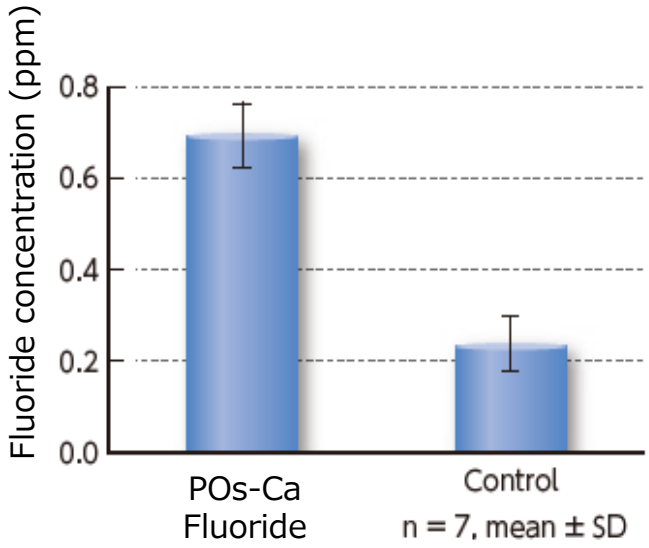
Bioavailable calcium and fluoride ions in saliva

Expediting remineralization and recrystallization and strengthening of enamel by calcium and fluorides ions





Golden ratio 1.67

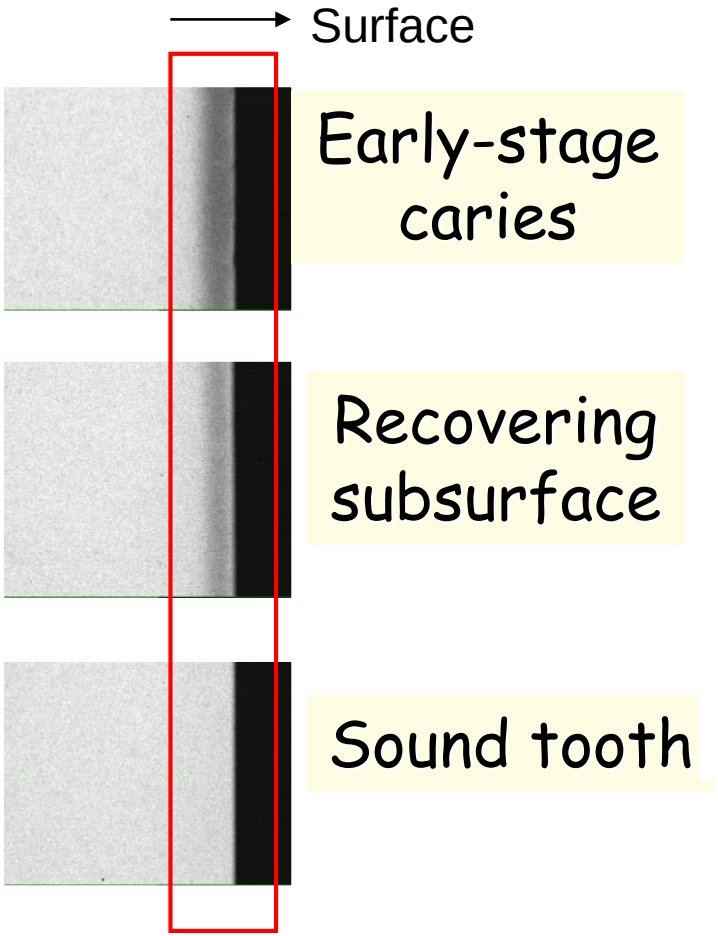


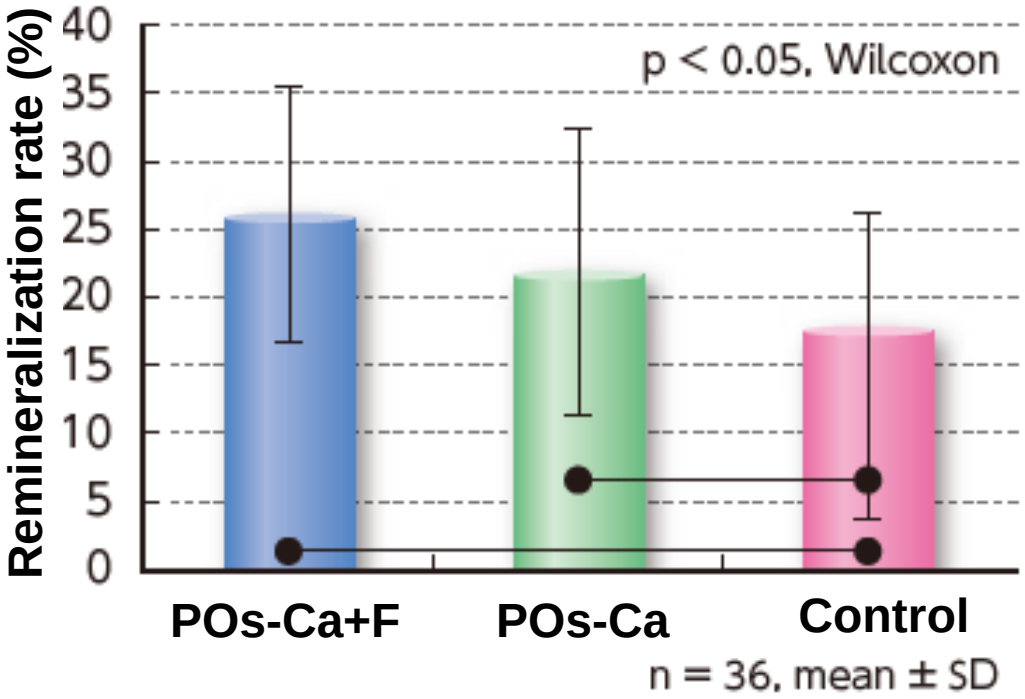
Same environment → Water fluoridation

Ca from POs-Ca + **F**luoride from tea extract

Remineralization of early-stage caries by “POs-Ca”

Analysis method: Transversal microradiography

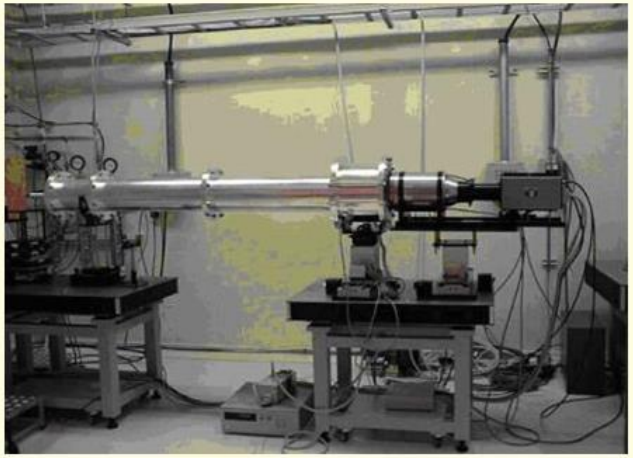


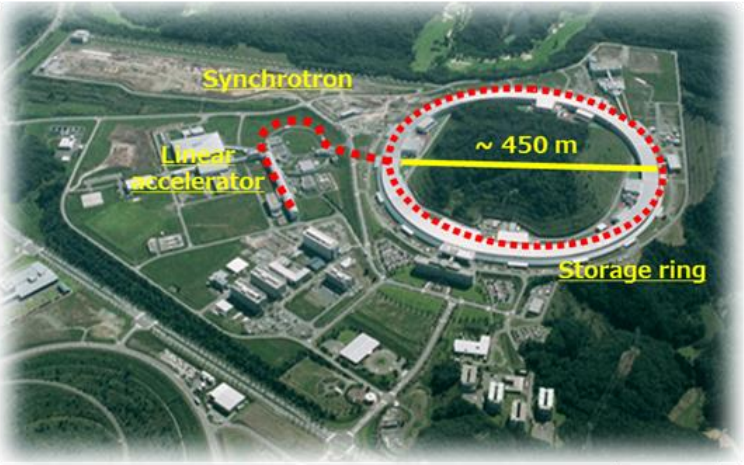


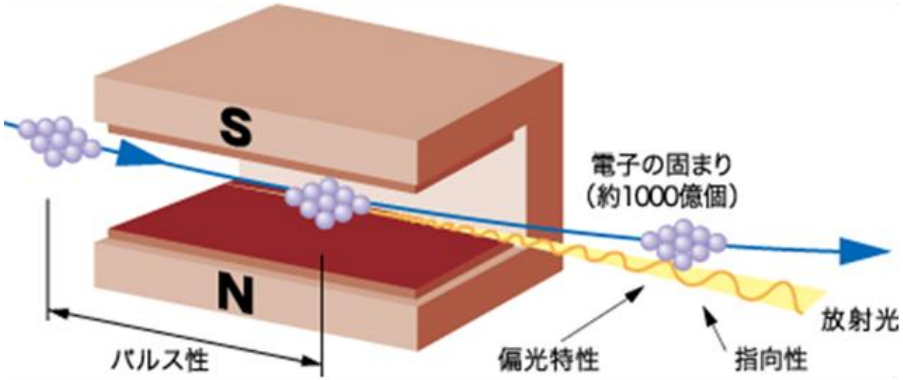
Kitasako et al. *J. Dent*. (2011)

POs-Ca+F and POs-Ca gums enhanced remineralization more effectively than control gum.

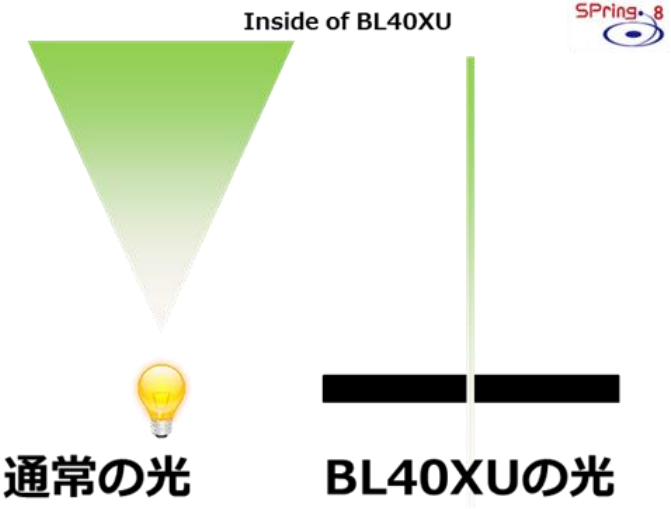
② New method



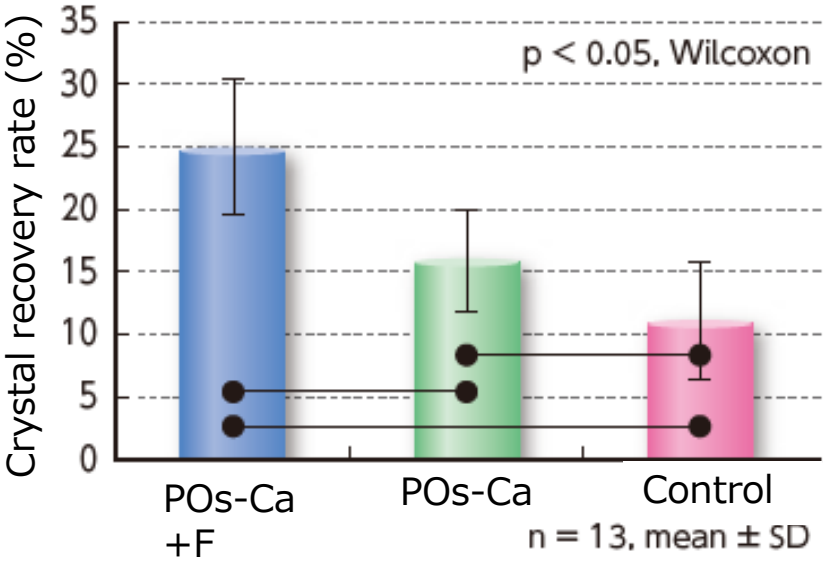




太陽光の1億倍の輝度

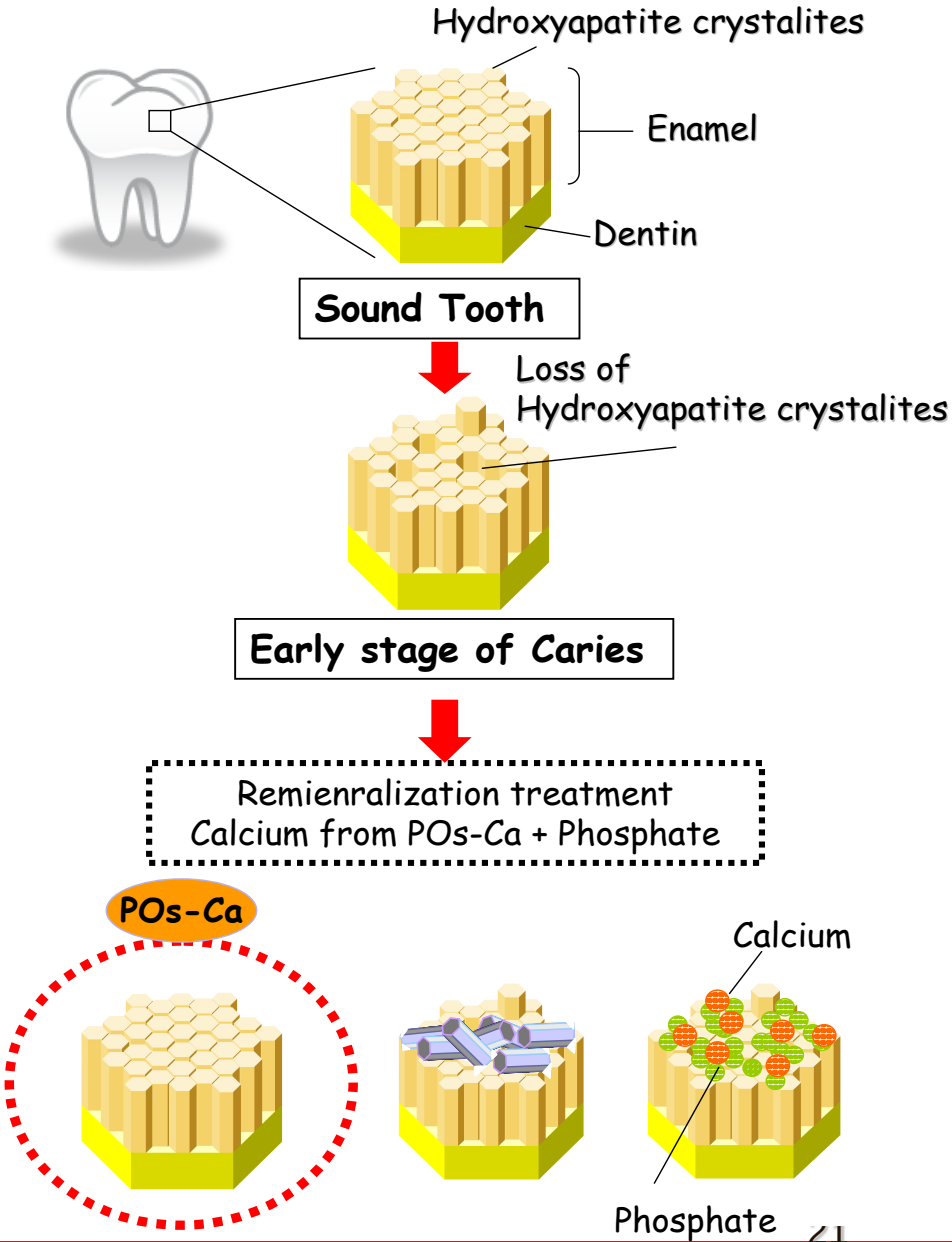


“Recrystallization” by POs-Ca gum



Kitasako *et al. J. Dent.* (2011)

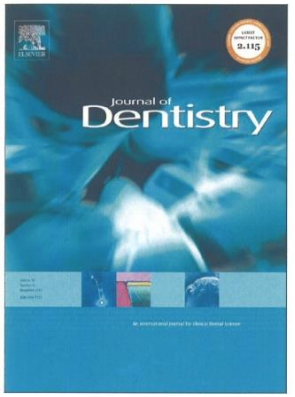
POs-Ca prevents early-stage caries at the nano level (crystal).



FOSHU health claim of “POs-Ca” chewing gum

Three experimentally-verified effects of POs-Ca (**3Rs**).

- **Re-mineralization** *J. Dent* (2011)
- **Re-crystallization** *J. Dent* (2011)
- **Re-hardening** *J. Dent. Res* (2012)



Early-stage tooth decay begins with demineralization. This product (“POs-Ca”) contains **phosphoryl oligosaccharides of calcium**. The calcium ion permeates teeth, then regulates the oral environment to **enhance remineralization and recrystallization of demineralized region**, and maintains strong and healthy teeth.

More credible and valuable product than any other chewing gums, for our current and *potential* customers.

The chewing gum containing POs-Ca

Recommended Chewing gum by Japan Dental Association

Measures for early caries lesion (↑Health claim, its was allowed by Consumer Affairs Agency, Government Of Japan)

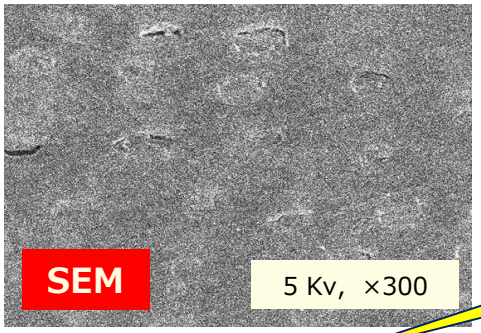
FOSHU* mark

FOSHU is only food products to claim of its function for health.

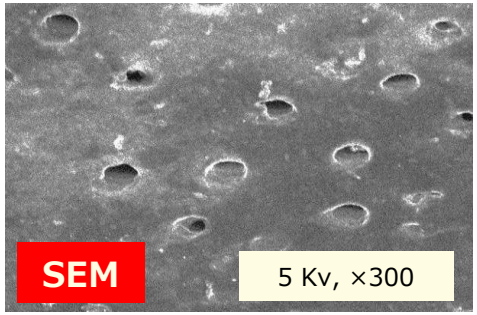
おいしさと健康
Glico

For hypersensitivity

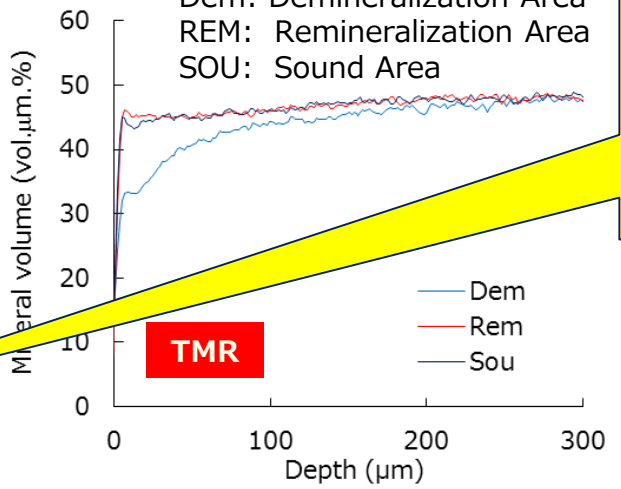
POs-Ca

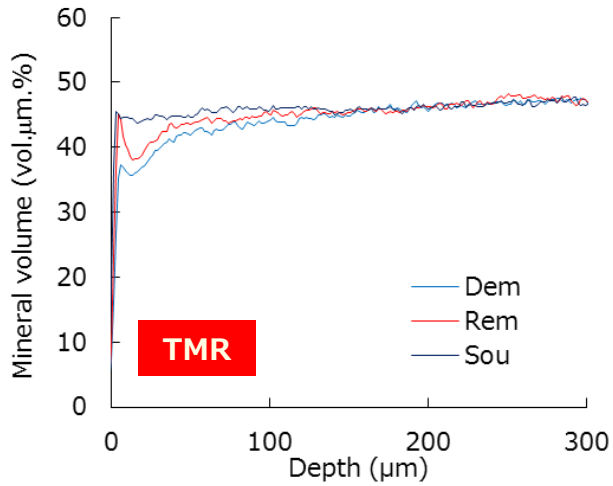


$CaCl_2$

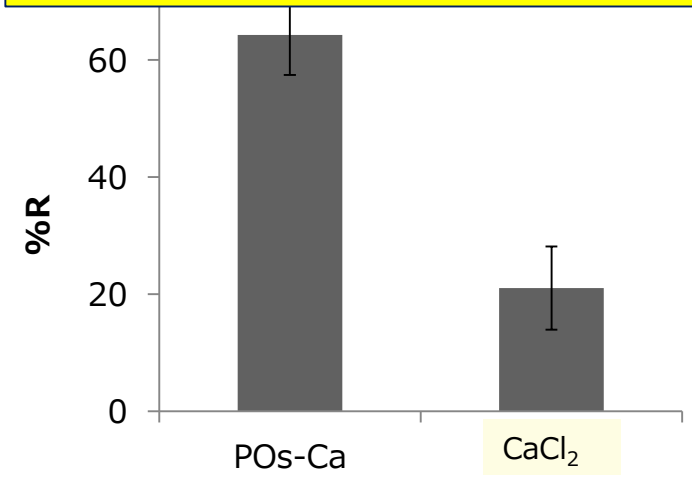


Dem: Demineralization Area
REM: Remineralization Area
SOU: Sound Area





The high soluble calcium "POs-Ca ®" has perfect occluding of the exposed dentin tubules



The rates of remineralization were 64.3±6.8% by POs-Ca and 21.0 ± 7.1% by $CaCl_2$ to mineral loss. (Mean ± SD, $p<0.05$,t-test)

The high soluble calcium "POs-Ca ®" has the ability enhanced remineralization and perfect occluding of the exposed dentin tubules of early caries lesions of dentin by liquid.

POs-Ca

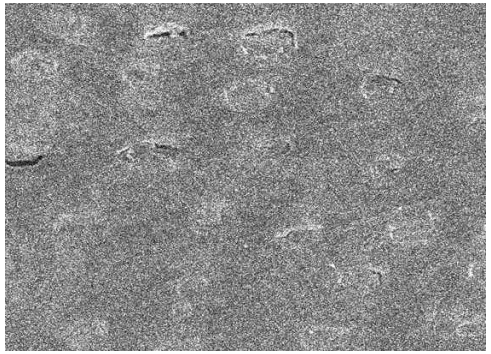


Fig.1-1. Surface

5 kV, ×300

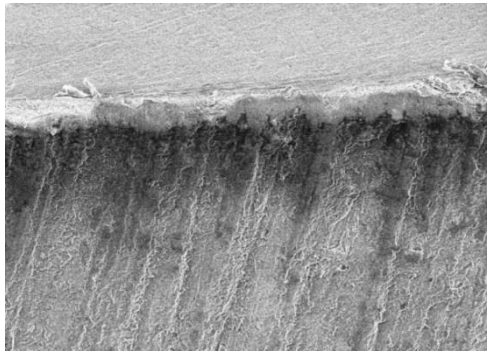


Fig.1-2. Cross-section surface

$CaCl_2$

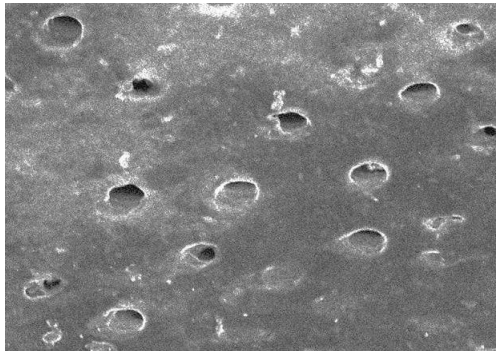


Fig.2-1. Surface

5 kV, ×300

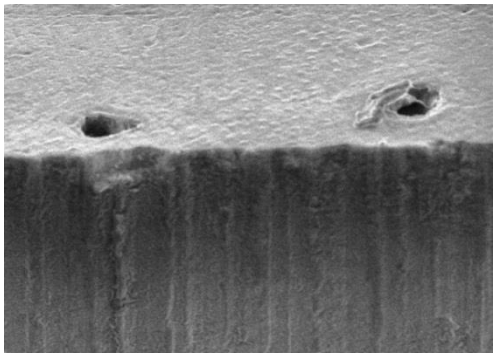


Fig.2-2. Cross-section surface

The list of safety tests for POs-Ca

- Acute oral toxicity test
- 28-days repeated dose toxicity test
- 90-days repeated dose toxicity test
- Reverse mutation assay “Ames Test”
- In Vitro Mammalian chromosome aberration test
- Acute dermal irritation test
- 14-days repeat application dermal irritation test
- Skin sensitization test
- Acute eye irritation test
- Oral mucosa irritation test of hamsters
- Human patch test

A wholesome life the best of taste

28