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**Mandar Todkar**
Assistant Professor, Department of Public Health Dentistry, M.A. Rangoonwala College of Dental Sciences and Research Centre, Pune, Affiliated to MUHS University, Maharashtra, India

**Renuka Nagarale**
Associate Professor, Department of Public Health Dentistry, M.A. Rangoonwala College of Dental Sciences and Research Centre, Pune, Affiliated to MUHS University, Maharashtra, India

**Samiksha Anjarlekar**
Undergraduate, Department of Public Health Dentistry, M.A. Rangoonwala College of Dental Sciences and Research Centre, Pune, Affiliated to MUHS University, Maharashtra, India

**Satyajit Muluk**
Undergraduate, Department of Public Health Dentistry, M.A. Rangoonwala College of Dental Sciences and Research Centre, Pune, Affiliated to MUHS University, Maharashtra, India

**Rufiyat Nadkar**
Undergraduate, Department of Public Health Dentistry, M.A. Rangoonwala College of Dental Sciences and Research Centre, Pune, Affiliated to MUHS University, Maharashtra, India

**Gursimran Singh**
Undergraduate, Department of Public Health Dentistry, M.A. Rangoonwala College of Dental Sciences and Research Centre, Pune, Affiliated to MUHS University, Maharashtra, India

**Gursimran Singh**
Undergraduate, Department of Public Health Dentistry, M.A. Rangoonwala College of Dental Sciences and Research Centre, Pune, Affiliated to MUHS University, Maharashtra, India

**Corresponding Author:**
**Samiksha Anjarlekar**
Undergraduate, Department of Public Health Dentistry, M.A. Rangoonwala College of Dental Sciences and Research Centre, Pune, Affiliated to MUHS University, Maharashtra, India

# Food fortification with anticariogenic agents: A comprehensive review

**Mandar Todkar, Renuka Nagarale, Samiksha Anjarlekar, Satyajit Muluk, Rufiyat Nadkar and Gursimran Singh**

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## Abstract
Several nutrients have been added to food and drink products around the world, as public health measures and as cost-effective ways of ensuring the nutritional quality of the food supply. Food fortification is a process of adding micronutrients which are necessary to prevent micronutrients deficiency, diseases related to it. Cariogenicity is one of the most common disease found in oral cavity all over the world irrespective of age group. So, to overcome this dental issue in mass population food fortification with anticariogenic agent is one of the amiable method. Anticariogenic agents like calcium sucrose phosphate ions, calcium glycerophosphate, sodium dihydrogen phosphate, casein phosphopeptide and amorphous calcium phosphate (CPP-ACP), commercial casein hydrolysate, etc. are used in food fortification. Food items like flour, soft drinks, salt, milk, sugar, chewing gum, bread, hard cheese, etc. are fortified with anticariogenic agents. This study is done to understand the importance, the methods and the agents of food fortification.

**Keywords:** Anti-cariogenic agents, dental caries, enamel, food fortification, micronutrients

## Introduction
Food fortification or enrichment is the process of adding micronutrients (essential trace elements and vitamins) to food. It is a proven, safe and cost-effective strategy for improving diets and for the prevention and control of micronutrient deficiencies. It can be carried out by food manufacturers or by governments as a public health policy which aims to reduce the number of people with dietary deficiencies within a population. As defined by the World Health Organization (WHO) and the Food and Agricultural Organization of the United Nations (FAO), fortification refers to "the practice of deliberately increasing the content of an essential micronutrient, i.e. vitamins and minerals (including trace elements) in a food, to improve the nutritional quality of the food supply and to provide a public health benefit with minimal risk to health", whereas enrichment is defined as synonymous with fortification and refers to the addition of micronutrients to a food which are lost during processing [1]. Food fortification is a scientifically proven, cost-effective, scalable and sustainable global intervention that addresses the issue of micronutrient deficiencies [2]. Cariogenicity is one of the most common disease found in oral cavity all over the world irrespective of age group. Globally, it is estimated that two billion people suffer from caries of permanent teeth and 520 million children suffer from caries of primary teeth [3]. As like food fortification with nutrients like vitamins and minerals we can used anti-cariogenic agent for fortification of food. Anticariogenic agents like calcium sucrose phosphate ions, calcium glycerophosphate, sodium dihydrogen phosphate, Casein phosphopeptide and amorphous calcium phosphate (CPP-ACP), commercial casein hydrolysate, etc. are used in food fortification. Food items like flour, soft drinks, salt, milk, sugar, chewing gum, bread, hard cheese, etc. are fortified with anticariogenic agents [4, 5, 6, 7]. The purpose of present review was to evaluate the effects of food fortified with anticariogenic agents and prevention of dental caries.

## Methods
The present review literature search was done using online and offline mode. The literature

consisted of different articles, textbook, studies, etc. The keywords used for the search were “Anti-Cariogenic Agents”, “Dental Caries”, “Enamel”, “Food Fortification”, “Micronutrients”, etc. The objective of review was to evaluate effectiveness of anti-cariogenic agents in food fortification. The only literature from English language was selected. No patient was involved in the present review.

**Food Fortification**

Food fortification process has been in practice since ages. Nutrient supplementation of foods was mentioned for the first time in the year 400 B.C. by the Persian physician Melanpus, who recommended adding iron filings to wine to increase soldiers’ “potency.” In 1831 the French physician Boussingault urged adding iodine to salt to prevent goitre. Food fortification became common during the first and second world wars to help prevent nutritional deficiencies within the population and to replace nutrients that were lost during food processing. Thus, during this period the adding of iodine to salt, vitamins A and D to margarine, vitamin D to milk, and vitamins B1, B2, niacin, and iron to flours and bread was established [8].

**Types of Fortification**

Types of food fortifications are mass fortification, target fortification, market driven fortification. In mass fortification we fortify foods that are widely consumed by the general population, such as cereals, condiments and milk. It is usually instigated, mandated and regulated by the government sector. Target fortification is used to fortify foods designed for specific population subgroups, such as complementary foods for young children or rations for displaced populations. E.g. school feeding programmes, special biscuits for children and pregnant women, and rations (blended foods) for emergency feeding and displaced peoples. Market driven fortification allows food manufacturers to voluntarily fortify foods available in the market place. Examples include certain minerals (e.g. iron, calcium) and sometimes selected vitamins (e.g. vitamin C, vitamin B2) [9].

**Methods of Food Fortification**

Methods of fortifications are commercial and industrial fortification. (e.g. wheat flour, corn meal, cooking oils), biofortification. (e.g. breeding crops to increase their nutritional value, which can include both conventional selective breeding and genetic engineering) and home fortification. (e.g. vitamin D drops) [10].

**Food Fortification in India**

Food fortification is used in many countries for improving nutritional value of that specific food item. India’s history of fortification began in 1953 when fortification of hydrogenated vegetable oil (vanaspati) with vitamin A and D was mandated. Mandatory salt iodisation began in 1998. However, in 2005-2006, only 51% of households utilized tolerably iodized salt [11]. The Indian government has recommended food fortification in the 10th, 11th, and 12th five-year plans as a strategy to improve nutrition through Indian Journal of Community Health 2014. Existing government nutrition programs are Integrated Child Development Services (ICDS) which targets pre-school children and pregnant and lactating women), MidDay Meal (MDM) which targets school children and Public Distribution System (PDS) which targets poor, underserved communities, provides fortified food on mass scale [12, 13, 14].

**Nutrition and Dental Caries**

Nutrition deficiencies can cause pre-eruptive and post-eruptive defects in tooth structure. Enamel maturation, physical and chemical composition, time of eruption, tooth morphology and size are all affected by pre-eruptive nutrient intake. Mineral malnutrition due to inadequate quantities of calcium, phosphorus and iron is also important factor for caries resistance. The dental dysplasia’s associated with malnutrition are odontoclasia in deciduous dentition, yellow teeth in permanent dentition, infantile melanodontia in deciduous dentition, linear hypoplasia in deciduous incisors (due to ascorbic acid and vitamin A deficiency or neonatal infection), enamel hypoplasia due to hypocalcaemia, pulp stone formation or atopic calcification in dentin is occurred by L-Ascorbic acid deficiency, hypoplastic lesions of enamel due to vitamin D deficiency. These defects can lead to extensive dental caries. Post eruptive effects of malnutrition are particularly due to malnutrition leads to decrease in salivary lysozymes and secretory IgA levels. Any alteration of salivary protein could have negative effects on the susceptibility of caries. Changes in salivary perioxidase, lactoferrin, lysozyme and other proteins can reduce the host defence mechanism to cariogenic organisms [15].

**Anticariogenic Agents used for food fortification**

Anticariogenic agents used for food fortification are calcium sucrose phosphate, potassium phosphate, calcium sucrose phosphate, calcium glycerophosphate, sodium dihydrogen phosphate, commercial casein hydrolysate, casein phosphopeptide and amorphous calcium phosphate (CPP-ACP), dicalcium phosphate, 0.1,0.2 or 0.4% disodium hydrogen citrate, lactobacillus rhamnosus GG (LGG),etc [4, 5, 6, 7]. Calcium sucrose phosphate is a mixture of calcium sucrose mono and diphosphate, disucrose monophosphate and inorganic calcium phosphate that contains 11% calcium, 9.5% organic phosphate and 2.5% inorganic phosphate. CaSP leads to an increase in the salivary calcium level and plaque-reducing ability. It may function in 3 ways: It may slow down the rate of acid solubility of enamel and increase rate of remineralisation by a common ion effect, it may inhibit formation of plaque and its adherence to enamel surface. It may inhibit acid producing process in plaque. Calcium sucrose phosphate contains bicarbonates, phosphates, and proteins have a buffer role in the saliva environment which prevents caries formation. Calcium glycerophosphate contains calcium glycerophosphate as an active ingredient. While taking it as a dietary mineral supplement, it helps maintain the level of calcium in the body. Thus, it helps in treating calcium deficiency, improving bone mineral density. Sodium dihydrogen phosphate ($NaH_2PO_4$) leads to sparing the enamel phosphate during bacterial carbohydrate mechanism; an enhanced buffering capacity in immediate environment of tooth; or common ion effect [4].

A casein hydrolysate containing enriched CPPs leads to the prevention of acidosis via suppression of lactic acid production. Casein phosphopeptide and amorphous calcium phosphate (CPP-ACP) is a successful sugar-free anticariogenic compound sequestrated from milk protein casein complexed with calcium phosphate. The Ser (P)-Ser (P)-Ser (P)-Glu-Glu sequence of CPP-ACP compound is responsible for the exceptional stability of calcium phosphate ions thereby encouraging the remineralisation process. This compound is also known to ameliorate the salivary pH and buffering capacity. Furthermore, CPP-ACP destroys the plaque bacteria bridging by competing for the calcium that is necessary for the bond. Also CPP can decrease s.mutans count with its ability to integrate in pellicle [6]. The fluoride increase caries resistance may arise from both systemic and topical applications of fluoride. Mechanisms of action of fluoride are increase enamel resistance or reduction in enamel solubility, increased rate of post-eruptive maturation, remineralisation of incipient lesions, interference with plaque microorganisms, and modification in tooth morphology [15]. Dicalcium phosphate has remineralizing or anticarious potential. Polyunsaturated fatty acids such as omega-3 and omega-6 fatty acids comprise 2 important classes of PUFAs that are most commonly represented by alpha-linolenic acid and linoleic acid, respectively [5]. Calcium and phosphate ions act as inhibitors for tooth erosion would operate by a 'buffering action'. Buffering agents maintain the pH at a level near neutrality, or safely above the value at which it could be responsible for any erosion. 0.1, 0.2 or 0.4% disodium hydrogen citrate stimulates salivary flow by citrate may lead to quicker clearance of acid after an acidogenic challenge [16]. Lactobacillus rhamnosus GG (LGG) is one of the probiotics investigated for the prevention of dental caries. It has been shown to inhibit cariogenic mutansstreptococci [17].

## Fortified Food Materials with Anticariogenic Agents

There are various food materials fortified with anticariogenic agents such as flour with soluble phosphate, chewing gum with CPPs or commercial casein hydrolysate, cereals with soluble phosphate, fruit-based drinks with 0.1,0.2 or 0.4% disodium hydrogen citrate, frozen dairy desserts with polyunsaturated fatty acids. There are also some food materials with 2 or more anticariogenic agents such as milk with vitamin D and sodium fluoride [4, 5, 6, 7].

## Effectiveness of Food Fortification with Anticariogenic Agents

According to result of various experiments related to food fortification with anticariogenic agent: Fortified gum including CPPs extracted from commercial casein hydrolysate can be a useful medium for CPP release in the oral cavity during chewing. However, a further calcium addition is aimed at enriching the CPP fraction of commercial hydrolysate employed in fortified gum. Finally, an "omic" approach was a powerful tool for underlining the different CPPs released during mechanical and *in vivo* chewing [6]. The incidence of dental caries varied among the various types of cereals employed and the added phosphate eliminated the increased incidence of caries associated with the addition of cereal to the experimental diets and produced a substantial decrease in the incidence of dental caries below the normal control level [7]. Omega 3 or 6 fatty acid extracts from fish or oil from algae in dairy matrices can be used to prevent several oral infections or inflammatory diseases such as caries, periodontitis, gingivitis, mouth ulcers and halitosis, due to their antimicrobial activity against many oral pathogens [5]. Low concentrations of disodium hydrogen citrate it might help to buffer the acids in fruit-based drinks, by this means reducing their erosiveness. Citrate inhibits phosphofructokinase and impedes glycolysis in Streptococcus mutans and S. sanguis. Orange juice, with a relatively high level of 5.66 g citrate/l, was associated with a greater fall in human dental plaque pH after a 10% sucrose solution rinse than other fruit drinks containing lower levels of citrate [16, 18]. When used appropriately, fluoride is a safe and effective agent that can be used to prevent and control dental caries. Fluoride is needed regularly throughout life to protect teeth against tooth decay. The use of fluoride in sugar has been studied as a means of preventing caries in animal and human experiments and has provided promising results. As plaque bacteria ferment sugar to produce lactic acid which demineralises enamel, the presence of fluoride inhibits acid production and promotes remineralisation of enamel. Fortification with vitamin D shows decrease in tooth decay as well as reduction in periodontitis [17].

## Technical Issues

Food science and technology play a key role with respect to several issues. For example, it is necessary to maintain the overall quality of the product in terms of the bioavailability of the fortifying agent. Although bioavailability may increase, the product's quality is at risk, especially its stability. It may be affected as colour, taste, odour, and appearance, alterations that should be avoided altogether since they affect consumer acceptability of the product [2]. The agent should not react with other components in the product [16]. The agent should neither be destroyed nor produce any harmful by products [19].

## Recommendations

1. We can use anticariogenic agent food fortification for prevention of dental caries as it is effective and has minimum disadvantages.
2. Food fortification with anti-cariogenic agent can implement through various government schemes which are providing other nutrient fortified food for specific age group according to need.

## Conclusion

Many of these substances will not interfere with food flavour and acceptance. These modifications require no change in food habits as well as product cost is nominal. Hence, we can use these fortified food items to prevent dental diseases.

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