

osteomalacia in adults. Calcium in the form of calcium salt such as calcium carbonate, calcium chloride, and calcium citrate are used as fortificants [18]. Some of the foods fortified with calcium include fruit and juice beverages, cereals, and snack bars [19].

- **Vitamin A:** Vitamin A is an important micronutrient used to cure night blindness, supports the immune system, and lowers the risk of cancer. Vitamin A is fortified with food such as cookies and pasta with vitamin A fortificant retinyl acetate [20]. Some of the foods fortified with vitamin A include edible oils and fats, condiments, refined sugar [21].
- **Dietary Fibers:** Fiber is important nutrients which help in constipation problems. Long-term constipation has serious health problems. Food fibers can be classified into two types which are soluble and insoluble fibers. There are more medical advantages in strands including keeping up with intestinal, controlling glucose levels, controlling glucose level. Fortification form of fibers are plant sources such as guar gum is used to fortify yogurt [22], noodles [23] and inulin can be used in processed meat products such as sausages [24].
- **Zinc:** Zinc is the essential nutrient required for growth, immune system, and pregnancy. It helps in the development of children with stunted growth and diseases such as diarrhea and pneumonia. The most common fortificants used for zinc are zinc oxide and zinc sulfate [25]. The study of biofortification of zinc to bread wheat grain focused on three different methods: soil application, seed priming, foliar spraying for biofortification of crops. The addition of zinc to bread wheat grain through methods mentioned

increased the grain zinc concentration of wheat [26].

Current Vitamin D Fortification Status: Fortification programs for vitamin D have been implemented in the world. Fortification of vitamin D depends on the availability and consumption pattern of food in the population of a country. Mainly food fortified with vitamin D includes milk, dairy products, edible oil, and fruit juices. Since vitamin D is a fat-soluble vitamin, it is also fortified with other fat-soluble vitamins such as vitamin A [27]. Many countries have reported successful fortification programs for vitamin D and further adopted regulatory compliance for vitamin D fortified food. It has become mandatory by the Canadian Food and Drug Regulations to fortify milk (except goat milk and condensed milk) and margarine [28]. In the USA, food fortified with vitamin D has to be displayed on the labels [29]. In some countries such as the UK and Ireland, it is voluntary to fortify margarine manufactured for domestic use [30]. Globally, all infants up to 1 year of age should receive a daily dose of 400 IU/day (10 µg) of vitamin D [31]. The recommended dietary intake for children and adolescents (up to 18 years of age) of vitamin D is 600 IU/day [32]. Fortification of vitamin D for infants were found in the following products: Cereal based baby porridge, soy milk, infant milk, follow-on formula, infant formula, yogurt drink, instant chocolate milk, curd cheese dessert and fruit juices [33]. In the world, food products that are being fortified with different levels of vitamin D are listed in Table 2. Some food products such as dried and evaporated milk, breakfast cereals, macaroni, noodles, beverages, edible oils, and wheat flour are also fortified with vitamin D along with other micronutrients. However, there is a challenge in

managing the continuation and compliance of the regulations for fortification. Also, the key concern for food processors is to study the stability, dispensability, and solubility of vitamin D during the production and storage of foods [34].

Role of Vitamin D in COVID-19: Vitamin D deficiency is a worldwide public health issue that affects more than a billion individuals of all age groups [35]. Several studies in the last decade have found a link between vitamin D deficiency and a variety of disorders, including systemic infection. [36-38]. Vitamin D deficiency has an impact on immune functioning because it acts as an immunomodulator [39], boosting innate immunity through the production of antiviral peptides [40], which increases mucosal defenses. In clinical investigations, low levels of serum vitamin D have been linked to acute respiratory tract infections, particularly epidemic influenza [41-42]. According to a recent meta-analysis that included data from eight observational studies, persons with a blood vitamin D content of less than 50 nmol/l (i.e., less than 20 ng/ml) had a 64% increased risk of community-acquired pneumonia [43]. Some recent reviews hypothesized that insufficient vitamin D may damage the immune function of the respiratory tract, increasing the severity of COVID-19 and the risk of death [44-45]. Some retrospective studies have determined the correlation between vitamin D levels and the severity and mortality of COVID-19 [46-50]. The outbreak and rapid spreading of SARS-CoV-2 is a global health threat with an uncertain outcome in the world. Recent data reported the antiviral effects of vitamin D, which has been shown to hinder viral replication directly, as well as has anti-inflammatory and immunomodulatory properties [51]. It seems that SARS-CoV-2

predominantly uses the immune evasion process during infection, followed by hyper reaction and cytokine storm in some patients [52], which is a known pathogenic pathway in the development of acute respiratory disease syndrome (ARDS) [53]. SARS-CoV-2 enters alveolar and intestinal epithelial cells via using angiotensin-converting enzyme 2 as the host receptor [54]. Subsequent dysregulation of the renin-angiotensin system may lead to excessive cytokine production resulting in potentially fatal ARDS [53].

Bioaccessibility and Stability of Vitamin D: Today, as per the latest medical reports available, much of the population throughout the globe is facing vitamin D deficiency. Other than the sunlight, there are very limited sources of vitamin D to fulfil the recommended dietary allowance of vitamin D (RDA: 400-800 IU per day) [55]. A large proportion of vitamin D is lost during food processing and storage due to environmental stress conditions such as temperature, pH, salt, oxygen, and light. Vitamin D deficiency can be corrected and prevented by sun exposure, increasing the dietary intake of vitamin D and reducing the underlying factors that hinder adequate absorption and utilization [56]. Periodic distribution of high dose vitamin D supplements seems to be an alternative option. However, its sustainability is questionable for many reasons: (i) gradual loss of interest by the target population (ii) difficult to ensure a continuous and adequate supply of the supplements and maintain an efficient distribution system [57]. To meet the RDA requirements for vitamin D, several countries have now permitted fortification of food with vitamin D such as milk, edible oils, cereals etc. In addition to this, currently, certain pharmaceutical supplements are also majorly being used as the source of vitamin D [58].

Despite the availability of vitamin D fortified food, vitamin D deficiency is prevailing across the globe which could be attributed to the low bioavailability of vitamin D (fortified as well as naturally occurring foods) in the food as well as in the human gastrointestinal tract (GIT) [59]. According to a research report published by the FAO, extended storage of vitamin A-fortified flour under severe conditions such as high temperature and improper packaging leads to an 85% loss in vitamin A activity within 3 months of storage [60]. Even with food fortification, intake of vitamin D is inadequate to obtain and maintain target 25(OH)D concentration of at least 30 ng/mL (75 nmol/L), and some of the modes used to generate fortified food do not reach those who need them (e.g., rice) [61]. Though several pharmaceutical formulations have been introduced to correct the imbalance, these formulations do not become healthy alternatives due to cost associated, out of reach to the public and their psychological impact as well as their adverse effect on health. Vitamin D is a fat-soluble vitamin, and its stability is determined by the fat medium in the fortified diet. Due to the volatility and varied dispersion of vitamin D in food, its fortification poses a significant problem to the food industry. Foods supplemented with vitamin D, such as milk, cheese, and yogurt, have been found to have lower vitamin D retention [62]. Food processing methods such as baking, cooking, frying, and boiling degrade vitamin D significantly. There are very few studies on the stability and uniform distribution of vitamin D fortified meals [63].

Technologies used for Vitamin D fortification: For the fortification of vitamin D, there are various techniques which include emulsification, microencapsulation, and

nanoencapsulation. Direct addition of vitamin D is mainly adopted for milk and milk products [46]. In this method, vitamin D is dissolved in food-grade organic solvent (ethanol) and butter oil and then homogenized into the food matrix to ensure the uniform distribution in milk [64-65]. It has been found that there is a deposition of vitamin D inside the packaging materials especially the poly packs or tetra packs and degradation in the aqueous food matrix led to instability of vitamin D in the food matrix. In the emulsification method, vitamin D acts as a water phase and is dispersed in the oil phase as fine droplets and then mixed with food products such as cheese, milk, and bread [66-67]. The major challenges found in the fortification of vitamin D by the emulsification method is the availability of food-grade emulsifiers and the development of stable emulsion in the food matrix. Dispersibility, homogeneity, stability are a few challenges that affect the vitamin D bioavailability to the body. Various innovative techniques came up with time which includes microencapsulation through nanotechnology. This method offers better stability and homogeneity by encapsulating the bioactive material in the food matrix at less than 1000 nm size. According to the literature, fortification using nanoparticles has several advantages over direct addition and emulsification methods, including increased stability, homogeneity, and improved physicochemical and organoleptic properties [68].

Nanoencapsulation Technique: Nanoencapsulation is the entrapment of bioactive compounds within a nanoscale carrier and is considered as an appropriate technology to overcome the bioavailability or bioaccessibility of the bioactive compound. This technique increases bioactive solubility, enhances release

behavior, cellular uptake, and bioavailability [69-73]. The selection of appropriate shells and methods for nanoencapsulation is an important and interesting field of research. The applied shell for entrapment of food bioactive should meet some criteria such as biocompatibility and biodegradability. Abundantly available starch is one of the good candidates to produce nano-delivery systems. It causes slow-release, inhibition of inadvertent release, reducing probable complications due to overdose and more effectiveness of sensitive ingredients [74-76]. The starch structure is known as a “double helix” [77] that consists of two types of molecules: the linear and helical amylose and the branched amylopectin [78]. The natural and spontaneous tendency of amylose to form single helical molecular inclusion complexes is termed V amylose [79-82]. It has a central hydrophobic cavity interconnected by amorphous regions of the polysaccharide chains which render the complexes stable to acidic hydrolysis and may be used as a possible platform for the encapsulation of hydrophobic molecules [83-86]. The technology used for food fortification include nanosuspensions, nanoliposomes, nano emulsions, and cyclodextrin carriers. The coating materials used for encapsulation of fortificants includes starches, sugars, fats, gums, chitosan, gelatin, and maltodextrin [87]. The application and their complexes are developed using surfactants, clinkers, and chelating agents. Nanoencapsulation of fortificants can be done by two methods i.e., electro spinning (fiber-like fortificants) and electro-spraying (particle-like fortificants) [88]. Further, the technique of nanoencapsulation does not contribute significant changes in the physicochemical properties and rheological properties of fortified foods. Nanotechnology-based techniques are also helpful in

addressing challenges that include encapsulating hydrophobic fortificants into food [89].

Microencapsulation Technique: Microencapsulation is basically insulation of bioactive core material by secondary wall materials which protect the core from its external environment [90-92]. In addition to giving protection to the bioactive compound, it also helps in the controlled release of the encapsulant. Microencapsulation also promises that the nanomaterials so formed would ensure high bioavailability, water dispersibility and better homogeneity of the fortificant in the target food irrespective of the complexity of the food matrix [69]. It aids in the regulated release of encapsulants with great physicochemical stability, as well as protecting the bioactive component [90-92]. Microencapsulation additionally guarantees, regardless of the complexity of the food material [69]. It is an efficient way for delivering two or more micronutrients simultaneously in a stable and bioavailable form without interaction is by microencapsulation of nutrients in an inert but digestible matrix, separating them from other food components and other micronutrients added to food [93]. The benefits of microencapsulation of vitamin D in food products include blocking the passage for vitamin D into the food matrix; protects against environmental conditions such as moisture, oxidation, pH, temperature; ensures higher bioavailability by releasing encapsulated vitamin D in a regulated and targeted manner; does not affect the appearance, taste, and quality of the food matrix, thus maintains customer acceptability [94]. Microencapsulation can be done by using spray drying. This is one of the oldest techniques used for bioactive compounds encapsulation [95]. Spray drying involves the

dissolution of wall material and core material resulting in the formation of emulsion, followed by the process of homogenization, pumping of emulsion, atomization of emulsion and subsequent dehydration of the atomized droplets to yield microcapsule [96]. Vitamin D is needed to be homogenized in a dispersion containing wall materials (polymers). Then, the homogenized dispersion needs to be fed to the spray dryer and atomized by hot air that leads to the development of nanomaterials in consequence of water evaporation [97-100]. The encapsulation process is subjected to a range of factors like homogeneity of dispersion system, quantity, quality, and type of emulsifier used, feed rate, viscosity of dispersion system, pressure of hot air, the flow rate of hot air and inlet and outlet temperature [101-104].

Emulsification technique: Another technique used for fortification of food can be emulsification. It involves at least two immiscible phases (lipid and water) where one phase needs to be dispersed as small spherical droplets within another phase. Two types of emulsions, oil in water (O/W) or water in oil (W/O) are classified based on their spatial arrangement of two phases. These two immiscible phases need to be stabilized by surfactants and emulsifiers [105]. Several techniques of emulsions to develop vitamin D-nanomaterials using food-grade materials such as whey protein isolate (WPI) [106], casein [107], Medium-chain triglycerides (MCT), Zein and carboxymethyl chitosan [108], Tween 20 and casein [109], have been explored. The selection of emulsion methods for vitamin D encapsulation depends on various factors such as absence/presence of antioxidants, quantity, type of carrier oils, and surfactant.

Table 1: Different techniques used for the fortification in various food vehicles

Technology	Method	Fortificants	Food Vehicles	References
Mixing	Dry Mixing	Iron	Fish Sauce	[110]
	Ribbon Blender	Iron and Iodine	Edible Salt	[111]
Biofortification	Fertigation	Iodine	Spinach	[16]
	Foliar Spraying	Iodine	Potato, tomato	[112]
	Breeding	Vitamin A	Sweet Potato, Banana	[113]
	Breeding	Iron	Rice	[114]
	Soil Application and Seed Priming	Zinc	Wheat grain	[26]
	Transgenic	Iron	Rice, Potato	[115-116]
Microencapsulation	Spray Drying	Iodine	Edible Salt	[17]
	Extrusion	Minerals	Rice Kernels, Corn Based Snacks	[117]
	Spray Chilling	Iodine, Iron and Vitamin A	Edible Salt	[118]
	Coating	Calcium	Soy-milk	[119]
Nanoencapsulation	Electrospinning	Iron	Yogurt, Biscuits	[120]
	Nanoliposome entrapment	ω -3 PUFAs	Yogurt	[121]

Table 2: Vitamin D fortification level of different food groups in the world

Country	Food Name	Vitamin D fortification level for adults	References
United States of America	Milk	400 IU/ 946 ml	[29, 122- 123]
	Yogurt	89 IU/100 g	
	Margarine	89 IU/100 g	
	Cheese and cheese products	81 IU/30g	
	Enriched rice	550–2200 IU/kg	
	Breakfast cereals	350 IU/100 g	
	Enriched noodle	90 IU/100g	
	Orange juice	100 IU/240 ml	
	Malted Drink	123 IU/g	
	Soy Based Drink	140 IU /240ml	
Canada	Milk	300-400 IU/100g	[124-125]
	Infant formulas	530 IU/100 g	
	Meal replacements and supplements	300-400 IU/100g	
Australia	Fat spreads	220-640 IU/100g	[126]
	Breakfast cereals	100 IU/serving	
United Kingdom	Margarine	282–352.8 IU/100 g	[127]
	Bread	200 IU/100g	
	Orange Juices	1000 IU/240ml	
India	Milk	200 -300 IU/L	[128]
	Vanaspati	44 IU– 64 IU/100g	
	Edible oil	44 IU– 64 IU/100g	
Malaysia	Condensed milk	111 IU/100 g	[129]
	Bread	83 IU/100g	
	Breakfast cereals	333 IU/100g	
Philippines	Milk	≥973IU/L	[130]
	Margarine	3300 IU/kg	
Brazil	Dried skimmed milk	2000–2400 IU/kg	[131]

CONCLUSION

Vitamin D is important for the proper functioning of the immune system. The outbreak of the COVID 19 pandemic had a massive impact on the health and economy of the world. The pandemic has made people more concerned about their health and fitness. Vitamin D deficiency is very common in all age groups of humans which are mainly associated with viral respiratory tract infections. However, fortification is considered the most effective way to improve the uptake and availability of vitamin D. This review paper

discusses the various techniques such as emulsification, microencapsulation and nanoencapsulation used for fortification of vitamin D. Encapsulation of vitamin D protects against degradation before it reaches the target site in the body.

Microencapsulation provides desired functionality such as stability and homogeneity and overall better bioavailability of vitamin D. Nanoencapsulation is the latest technique used for fortification of vitamin D by maintaining stability during

thermal processing and storage. There is certainly wide scope to develop novel techniques for fortification of vitamin D with better stability and availability.

List of Abbreviations: ARDS: Acute Respiratory Disease Syndrome, WHO: World Health Organization, COVID: Corona Virus Disease 2019, UV: Ultraviolet, SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2, USA: United States of America, UK: United Kingdom, IU: International Unit, RDA: Recommended Dietary Allowance, GIT: Gastro-Intestinal Tract, FAO: Food and Agriculture Organization, WPI: Whey Protein Isolate, MCT: Medium Chain Triglycerides.

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