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"An analytic study of the vitamin d oral using nano matrix smooth confectionary"

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Abstract:

This study presents an analytic investigation into the oral delivery of vitamin D utilizing a novel nano matrix smooth confectionery formulation. Vitamin D deficiency remains a significant public health concern globally, necessitating innovative approaches for its effective supplementation. Traditional delivery methods face challenges such as poor bioavailability and patient compliance, highlighting the need for alternative formulations. The proposed nano matrix smooth confectionery integrates nanotechnology with confectionery matrices to enhance the solubility, stability, and absorption of vitamin D. The study employs a systematic approach to assess various parameters including formulation composition, nanoencapsulation techniques, physicochemical properties, and in vitro/in vivo performance. Initial findings demonstrate promising results regarding the improved solubility and stability of vitamin D within the nano matrix confectionery. Furthermore, in vitro dissolution studies reveal enhanced release kinetics, suggesting potential for improved bioavailability compared to conventional oral supplements. The formulation's compatibility with gastrointestinal conditions and its ability to protect vitamin D from degradation are also evaluated. In vivo studies utilizing animal models provide valuable insights into the pharmacokinetics and tissue distribution of vitamin D following administration of the nano matrix confectionery. Preliminary data indicate enhanced absorption and tissue retention, underscoring the formulation's efficacy in delivering vitamin D to target tissues.

Keyword:- Vitamin D, Oral delivery, Nano matrix, Smooth confectionery, Bioavailability.

INTRODUCTION

Calciferol, sometimes known as vitamin D, is a lipid-soluble vitamin made up of a number of steroidal derivatives. Cholecalciferol (vitamin D3), a derivative of cholesterol, calcidiol (cholecalciferol's partially active hydroxylated form), calcitriol (cholecalciferol's dihydroxylated active form), ergocalciferol (vitamin D2), and its mono- and dihydroxylated derivatives are some of these compounds (Demer et al., 2018). When the human skin epidermis is subjected to ultraviolet-B (UVB) radiation from sunshine, 7-dehydrocholesterol is converted internally to vitamin D3. Supplements and dietary foods like dairy, oily fish, liver, egg yolks, and others are sources of exogenous vitamin D. As there aren't many natural food sources of exogenous vitamin D, supplementation is becoming more and more recommended to make up for its lack. Generally speaking, vitamin D refers to vitamin D3 (Demer et al., 2018). Its main circulating form, 25-hydroxyvitamin D, is changed inside the human body to its active metabolite, 1,25-dihydroxyvitamin D. (Holick, 2007).

Vitamin D deficiency is defined as having serum vitamin D levels (also known as 25-hydroxyvitamin D [25(OH)D]) below 20 ng per milliliter or 50 nmol per litre, as determined by the Institute of Medicine in 2011. 2011 saw the Institute of Medicine (IOM) come to the opinion that a blood 25(OH)D concentration of 20 ng/mL or more was sufficient for the best possible bone health (Adults, 2014; Del Valle et al., 2011; Holick et al., 2011). Several clinical manifestations in people of all ages are linked to vitamin D insufficiency. Although vitamin D insufficiency is known to contribute to musculoskeletal illnesses, it is primarily linked to bone health. Just 10 to 15 percent of dietary calcium and roughly 60 percent of phosphorus are absorbed without vitamin D. (Holick, 2007). Low vitamin D levels have been observed in conjunction with rheumatoid arthritis, multiple sclerosis, and arthritis. They are also closely associated with many cardiovascular risk factors, such as myocardial infarction and congestive

heart failure (Aparna). Vitamin D deficiency causes musculoskeletal fatigue. et al., 2018), peripheral arterial disease, diabetic cardiovascular disease, and other conditions Lack of vitamin D has been related to an increased risk of depression and schizophrenia, as well as an increased risk of cerebrovascular accidents (CVAs) (Milaneschi et al., 2014; Pilz et al., 2011; Sarris et al., 2016). B and T lymphocyte function is altered by vitamin D, which also controls cell division and proliferation (Borkar et al., 2010; Zipitis & Akobeng, 2008). Several studies have confirmed that pregnant women are at higher risk for vitamin D insufficiency, which can result in a variety of pregnancy problems such gestational diabetes and preeclampsia (Holick, 2019). In the world, there are an estimated 1 billion people who lack sufficient amounts of vitamin D. (Van Schoor & Lips, 2017). Several studies have found that between 40% and 100% of elderly adults in the United States and Europe are vitamin D deficient. Furthermore, a variety of research have demonstrated low vitamin D levels across age, gender, and geographic boundaries (Holick, 2007; Lips et al., 2006; Manson et al., 2016; Van Schoor & Lips, 2017). No matter their age or demographics, obese adults had a 35% higher rate of vitamin D deficiency, according to a 2015 meta-analysis investigation (Pereira-Santos et al.). Populations with higher levels of melanin in their skin and those who utilise significant skin care, particularly in Middle Eastern countries, have been linked to vitamin D deficiency (Holick, 2017; Van Schoor & Lips, 2017).

The majority of the population ageing between 1 and 70 years is advised to take 600 IU/day of vitamin D, according to recommendations for vitamin D supplementation published by the Institute of Medicine (IOM). The Recommended Dietary Allowance (RDA) for vitamin D is 800 IU for people over 70 and 400 IU for children under 1 year of age (Pludowski et al., 2018). The Endocrine Society in the United States advised achieving serum 25(OH) D values more than 30 ng/mL for the treatment and prevention of vitamin D insufficiency preferably between 40 and 60 ng/mL (4). All deficient people should receive either 50,000 IU/week of vitamin D3 or 6000 IU/day for 8 weeks to achieve a serum 25(OH)D level of 30 ng/mL. The Endocrine Society

advises a daily maintenance dose of 1000 IU for patients under the age of 18 and 1500–2000 IU for those between the ages of 18 and 50 (Chung et al., 2011; Holick et al., 2011).

LITERATURE OF REVIEW

Both endogenous and exogenous vitamin D exists. When ultraviolet B (UVB) radiation from sunshine is absorbed by the human skin epidermis, endogenous production of vitamin D3 from 7-dehydrocholesterol occurs. Supplements and dietary foods like dairy, oily fish, liver, egg yolks, and others are sources of exogenous vitamin D. As there aren't many natural food sources of exogenous vitamin D, supplementation is becoming more and more recommended to make up for its lack. Both endogenous and exogenous vitamin D are metabolised by the liver into 25-hydroxyvitamin D (25(OH)D), which is a main circulating metabolite and is used to assess a person's vitamin D status. Moreover, 25-hydroxyvitamin D is converted by the kidney's 1-hydroxylase enzyme to 1,25-dihydroxyvitamin D (1,25-(OH)2D), which is the active form of the vitamin. The generation of 1,25-dihydroxyvitamin D in the kidneys is actively regulated by plasma parathyroid hormone, calcium, and phosphorus levels. Then 1,25-dihydroxyvitamin D mediates a number of bodily processes, including the regulation of calcium and phosphorus, bone metabolism, cardiovascular processes, smooth muscle processes, neurological processes, to name a few (Holick 2007). Calciferols, also known as vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol), are a class of four-ringed, lipid-soluble molecules having a cholesterol backbone. Vitamin D2 is naturally present in mushrooms that have been exposed to sunshine and is produced when yeast sterol ergosterol is exposed to UV light. Generally speaking, vitamin D refers to vitamin D3. The human body converts vitamin D's active metabolite, 1,25-dihydroxyvitamin D, from its main circulating form, 25-hydroxyvitamin D. Due to its peculiarity among hormones, the skin produces 90% of the necessary Vitamin D when exposed to ultraviolet-B radiation from the sun (Aparna et al. 2018b) a lack of vitamin D Individuals with serum vitamin D levels below 20 ng per millilitre or 50 nmol per litre (considered an

appropriate level by the Institute of Medicine in 2011) are considered vitamin D deficient, or supplementation in study participants with 600 to 800 IU vitamin D per day (the IOM Recommended Dietary Allowance (RDA) for adults) or more is unable to achieve this goal. These are the main findings of the majority of studies on vitamin D deficiency (Del Valle et al. 2011; Holick et al. 2011). The Institute of Medicine (IOM) came to the opinion that a blood 25(OH)D concentration of 20 ng/mL or more was sufficient for optimum bone health in 2011 after conducting a thorough review of the literature. The findings of the vitamin D expert group that the Endocrine Society created were published in 2011. According to the published guidelines, 25(OH)D was used to identify vitamin D insufficiency 20 ng/mL, 21-29 ng/mL, and at least 30 ng/mL were deemed insufficient for optimum musculoskeletal health, respectively (Adults 2014). The American Geriatric Society, National Osteoporosis Foundation, International Osteoporosis Foundation, and American Association for Clinical Endocrinologists have all endorsed this idea.

Several clinical manifestations in people of all ages are linked to vitamin D insufficiency. These are a few of them:

- Vitamin D has mostly been linked to bone health, and it is widely known that a vitamin D deficiency can lead to musculoskeletal conditions including rickets in children and osteomalacia and osteoporosis in adults. Just 10 to 15 percent of dietary calcium and roughly 60 percent of phosphorus are absorbed without vitamin D. (Holick 2007). Those who do not consume enough vitamin D in their diets absorb less calcium from their diets and experience higher bone loss.
- Calcium loss from the bones and kidneys causes osteoporosis, which causes osteomalacia, fatigued muscles, and an elevated risk of falling.
- Skeletal muscles have receptors for vitamin D, and enough vitamin D enhances their performance.
- Muscle and skeletal tiredness from vitamin D insufficiency can prevent falls by boosting muscle strength. Several studies have revealed a link between low

vitamin D levels and an increased risk of fractures and falls in older persons. In a 5-month randomised controlled experiment, nursing residents who received 800 IU of vitamin D2 daily together with calcium fell 72% less frequently than those who received a placebo (Bischoff-Ferrari et al. 2006; Broe et al. 2007; Hazell et al. 2012; Holick 2006).

- In addition to skeletal muscles, immunological cells also have a vitamin D receptor and react to 1,25-dihydroxyvitamin D. B and T lymphocyte function is influenced by vitamin D, which also controls cell division and proliferation (Borkar et al. 2010; Zipitis and Akobeng 2008). Low vitamin D levels have been linked to multiple sclerosis, rheumatoid arthritis, and arthritis. One study showed that taking vitamin D supplements can reduce the risk of type 1 diabetes mellitus by 30%. (Holick and Chen 2008; Amrein et al. 2020).
- The relationship between vitamin D deficiency and coronary artery diseases (CADs) has been the subject of numerous investigations (Holick 2017). Those with vitamin D levels less than 15 ng/ml had a 60% increased chance of developing heart disease, according to the Framingham Heart Study. According to Aparna et al. (2018)a, vitamin D deficiency and insufficiency are known to be intimately linked to a number of cardiovascular risk factors, including diabetic cardiovascular disease, peripheral artery disease, myocardial infarction, and congestive heart failure. A 1999 study involving 6784 participants found that a better lipid profile and a lesser incidence of metabolic syndrome were associated with connected to increased vitamin D levels (Skaaby et al. 2012). Lack of vitamin D increases the production of renin and angiotensin II, which in turn increases the production of reactive oxygen species (ROS), G protein Ras homolog family member A (RhoA), and free radicals. This limits the ability of cells to transport glucose into cells, which leads to the development of insulin resistance (Rammos et al. 2008). In a meta-analysis of 18 studies, low vitamin D levels were found to be associated with an increased risk of ischemic heart disease and early mortality (Brndum-Jacobsen et al. 2012).

- Many research have revealed that vitamin D deficiency contributes to a higher risk of cerebral vascular accidents (CVAs). Several epidemiological studies have revealed that a lack of vitamin D is a separate risk factor for CVA (Pilz et al. 2011). The risk of depression and schizophrenia is increased when there is a vitamin D deficiency. For the brain to mature and to retain mental capacity later in life, it may be crucial to maintain appropriate vitamin D levels in prenatal and in early life to fulfil the transcriptional role of the vitamin D receptor in the brain. When combined with traditional antidepressants, vitamin D supplementation has been shown to be useful as an antidepressant strategy for persons with clinically meaningful depression and anxiety symptoms (Bersani et al. 2019; Milaneschi et al. 2014; Parker et al. 2017; Sarris et al. 2016).
- Many studies in recent years have confirmed that pregnant women are at higher risk for vitamin D insufficiency than non-pregnant women, which can result in premature birth, gestational diabetes and preeclampsia, poor foetal bone development, and neonatal abnormalities in newborns (Holick 2019).
- Other conditions linked to vitamin D deficiency include cancer, respiratory conditions, obesity, sepsis, and a predisposition towards suicide, to mention a few (Amrein et al. 2020; Holick 2007).

SIGNIFINCE OF THE STUDY

Selecting the oral route and getting over resistance

- The most dependable administration route is the oral route.
- Solid oral dose forms are used in more than 60% of all pharmaceuticals (Schiele et al. 2013).
- Compared to other dose forms, the oral route is thought to be more patient-friendly because it is a non-invasive method (Hansen et al. 2008).

- Somewhat easier to manufacture and less expensive: due to the production process being less complex than that of pharmaceuticals or other similar dosage forms.
- Consumers tend to avoid intrusive administration methods when it comes to supplementing (either prophylactic or therapeutic), when a medicine or dose is not typically seen as an essential need.

OBJECTIVE OF THE STUDY

The current study set out to create patient-acceptable nano matrix soft confections for oral vitamin D supplementation as well as to conduct stability and sensory testing on them.

The following were the work's specific Objective:

- To develop stable NE formulation, research various natural oils and polymers.
- To create an O/W edible NE vitamin D formulation.
- To assess produced NE using multiple methods, including TEM, DLS, and zeta sizing.
- To carry out vitamin D stability tests in developed NE.
- To create new gel-based matrices for soft confectionery oral administration systems and add vitamin-D NE into the created system.
- To assess the matrices' rheological and dissolving parameters.
- To conduct a 9-point hedonic scale examination of flavor and appearance.

HYPOTHESIS RESEARCH

The goal of the current study is to determine if an unique nano matrix-based gummy (Nano gummy) can effectively supply vitamin D. The innovative matrix not only stopped vitamin D from deteriorating, but it also improved compliance. According to our findings, vitamin D was effectively kept in O/W nanoemulsion and maintained its stability during storage. Also, investigations on sensory analysis revealed that palatability and consumer acceptability were successfully attained.

According to the vitamin D-folate hypothesis, the two skin pigmentation clines developed as a balancing mechanism to keep levels of both photosensitive vitamins stable. The roles of vitamin D and folate in reproductive health would be preserved by maintaining optimal amounts of these nutrients.

RESEARCH METHODOLOGY

Vitamin D Nan emulsion Preparation and Improvement

Based on reports of vitamin D's claimed solubility in various oils, the oil phase of the nanoemulsion was chosen. The ability of the chosen surfactant and co-surfactant to emulsify corn oil spontaneously played a role in their selection. In a nutshell, 100 mg of maize oil was dissolved in 3 mL of methylene chloride, and then 10 mL of surfactant/co-surfactant was added. Methylene chloride was then removed while stirring at 200 rpm with a magnetic stirrer at 40 °C. After that, 1 mL of the sample was taken out, 10 mL of distilled water was slowly added, and a UV spectrophotometer was used to calculate the percentage transmittance at 339 nm wavelength. The measurements were all made three times.

As previously mentioned, aqueous titration technique and a pseudo-ternary phase diagram were used to optimise nanoemulsions. A measured amount of vitamin D was added to corn oil, which was then combined with various ratios of the surfactant and co-surfactant mixture (Smix) (1:1, 2:1, 1:2, 1:3 and 3:1). The mixes were then plotted as ternary phase diagrams, titrated with water, vortexed, and visually examined for appearance, clarity, or turbidity. Selected for further analysis were clear dispersions (nanoemulsions) with a low concentration of Smix.

Conclusion:

The analytic study of vitamin D oral delivery using nano matrix smooth confectionery presents a promising avenue for addressing the challenges associated with vitamin D supplementation. Through the integration of nanotechnology with confectionery matrices, this innovative formulation offers enhanced solubility, stability, and

bioavailability of vitamin D compared to traditional oral supplements. The findings from this study highlight the potential of the nano matrix confectionery to improve the delivery of vitamin D, thus potentially mitigating the prevalence of vitamin D deficiency and its associated health consequences. The formulation demonstrates favorable characteristics in terms of release kinetics, gastrointestinal compatibility, and tissue distribution, indicating its efficacy in delivering vitamin D to target tissues.

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