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عنوان المشروع باللغة العربية - Title of the proposed project in Arabic	تأثير مكملات فيتامين د عن طريق الفم على مستويات كربوكسي ببتيداز ان و أكسيد النيتريك في المرضى السعوديين
Title of the proposed project in English	Impact of oral vitamin D supplementation on serum Carboxypeptidase N and nitric-oxide levels in Saudi patients
المشرف الرئيس - PI	Prof. Nasser Al-Daghri
التخصص الدقيق للمشرف الرئيس - Specialty of PI	Clinical Biochemistry
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المدة المتوقعة لإنجاز البحث منذ الحصول على موافقة عمادة الدراسات العليا (بالشهور) - Expected time in month to finish	12 شهر
Abstract of the proposal (No more than 200 words)	Our aim was to study the correlation of Carboxypeptidase N and nitric-oxide levels with serum 25(OH)D in response to vitamin D supplementation in a Saudi population.

Hypothesis of the proposal	Vitamin D deficiency is high in the Kingdom of Saudi Arabia. Therefore, it is significant to recognize which biochemical markers modulate serum 25 hydroxyvitamin D 25(OH)D in response to vitamin D supplementation in such a population. Vitamin D is a secosteriod humans acquire from their diet, dietary supplements and exposure to sunlight. Upon ingestion or absorption through the skin, the biologically inert vitamin D3 is hydroxylated in the liver to form 25D [1,2]. In the kidney, 25D is further hydroxylated by the enzyme 25D-1α-hydroxylase into its active form, 1,25D [3]. The major circulating metabolite of vitamin D is 25D and blood levels serve as the best indicator for vitamin D status [4]. Since the kidneys tightly regulate the production of 1,25D, serum levels do not rise in response to increased exposure to sunlight or increased intake of vitamin D [1]. Carboxypeptidase N is synthesized by the liver and secreted into the blood where its concentration is high, approximately 30 µg/ml (10- 7 M) [5, 6]. As determined by Northern analysis (Tan and Skidgel, unpublished) [7], the liver is its only site of synthesis, however, only low levels of CPN can be extracted from the organ itself [8]. Probably it is not stored there, but secreted shortly after synthesis. Although some reports claimed the presence of CPN in tissues or non-hepatic derived cells [9], contribution of CPN from the blood in tissues or serum used to grow cells was not ruled out. The amino acid l-arginine is used by nitric-oxide synthases (NOS) to produce the biologically active gas nitric oxide (NO), which acts as a potent mediator of smooth muscle relaxation and as an inhibitor of platelet aggregation. Because the arginine concentration normally found in cells and plasma (100–800 M), is well above the Km value (1–20 M) for the constitutive NOSs (endothelial or neuronal NOS), it was first generally considered that the arginine supply was not a rate limiting factor for NO production. However, a variety of different model systems have demonstrated that increasing extracellular arginine does increase NO production [10]. Although this so called “arginine paradox” is poorly understood it may be partly due to the increased expression of the inducible NOS (iNOS) during inflammation. Little is known about the use of arginine for NO synthesis derived from peptides and proteins. However, during inflammation when iNOS is induced and the generation of free arginine is increased by the action of carboxypeptidases on numerous proinflammatory mediators, it is reasonable that NO levels may increase. This hypothesis has recently been supported by in vitro data using a macrophage cell line RAW 264.7 that expresses CPD [11]
Specific objectives	Our aim was to study the correlation of Carboxypeptidase N and nitric-oxide levels with serum 25(OH)D in response to vitamin D supplementation in a Saudi

	population.
Methodology & Major Techniques to be used	Spectropotometer, Cobas
Availability of Samples	Yes
Availability of Chemicals	Yes
Availability of Instruments	Yes
Ethical Approval	Ethical approval is available
Recent References	[1]. Holick MF, Garabedian M. Vitamin D: photobiology, metabolism, mechanism of action, and clinical applications. 6th ed. In: Favus MJ, ed. Primer on the metabolic bone diseases and disorders of mineral metabolism. Washington, DC: American Society for Bone and Mineral Research, 2006:129-37. [2]. DeLuca HF. Overview of general physiologic features and functions of vitamin D. Am J Clin Nutr 2004;80:1689S-96S. [3]. Bouillon R. Vitamin D: from photosynthesis, metabolism, and action to clinical applications. In: DeGroot LJ, Jameson JL, eds. Endocrinology. Philadelphia: W.B. Saunders, 2001:1009-28 [4]. Atkins GJ, Anderson PH, Findlay DM, et al. Metabolism of vitamin D3 in human osteoblasts: evidence for autocrine and paracrine activities of 1α,25-dihydroxyvitamin D3. Bone 2007;40:1517-28. [5] Erdös EG. Kininases. In: Erdös EG, editor. Handbook of Experimental Pharmacology, vol. 25. Heidelberg: Springer-Verlag; 1979. p. 427–87. Suppl

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