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Short Communication

Per, and -Polyfluoroalkyl Substances (PFAS): Human Vitamin D Deficiency and Blood Plasma Protein Binding

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Per and -Polyfluoroalkyl Substances (PFAS) are a class of chemicals which consist of more than 10,000 individual chemicals. They were developed in the 1930's and became in high demand in the mid 1940's with the development of Polytetrafluoroethylene (PTFE) also known as Teflon [TM]. Toxicological testing in the 1950's revealed that these compounds can bind to human blood proteins [1]. More recent studies [2] have demonstrated that several of these chemicals can cause carcinogenicity, developmental & reproductive toxicity, endocrine disruption, immunosuppression, increased cholesterol levels and interfere with Vitamin D Receptor (VDR) binding as well as interfere with other medications that bind to blood plasma proteins.

PFAS are predicted to be in the blood of approximately 98% of the United States population based on the National Health and Nutrition Examination Survey (NHANES) conducted by the Center for Disease Control and Prevention. A cross-sectional analysis of 7,040 individuals who participated in the NHANES survey [3] demonstrated that PFAS interfere with Vitamin D binding at the VDR site. Additional research on 5,254 PFAS to VDR, using molecular docking, molecular dynamics and free energy binding calculations [4] also indicated that "a large number of PFAS of commercial and regulatory importance may impact the function of the VDR and interfere with the beneficial effects of vitamin D3" leading to "increased osteoporosis and impaired immune function".

Concerns should also be raised for other medications that are known to exhibit high binding (>90%) to human plasma proteins. These would include drugs such as Acetazolamide, Amiodarone, Amitriptyline, Atovaquone, Bezafibrate, Bumetanide, Clindamycin, Diazepam, Dipyridamole, Dutasteride, Efavirenz, Felodipine, Finasteride, Furosemide, Gemfibrozil, Glipizide, Hydroxocobalamin, Ibuprofen, Indometacin, Levothyroxine, Lopinavir, Mefenamic acid, Montelukast, Naproxen, Phenytoin, Pioglitazone, Propranolol, Rivaroxaban, Spironolactone, Tacrolimus, Terbinafine, Tolbutamide, Verapamil, and Warfarin [5].

The dose and efficacy of these types of drugs are based directly on the amount of proteins available in blood for binding; if PFAS are already present in the blood and bound to blood proteins this will impact therapeutic benefits and potentially increase adverse reactions associated with these medications.

In summary, the data reported demonstrates the adverse reaction potential that can be caused by PFAS binding to blood proteins both In Vitro and In Vivo clearly establishing a "cause and effect" relationship between various PFAS chemicals and a variety of medications. This data should cause one to consider evaluating PFAS blood levels in individuals with moderate to severe Vitamin D deficiencies and/or in patients experiencing adverse reactions to medications competing with blood proteins and when appropriate, develop PFAS avoidance measures to reduce blood levels over time of these substances.

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