

CLINICAL SPECIFICATIONS

DINITROPHENYL

Chemical Found In:

Dinitrophenyl (DNP) is a chemical compound containing nitro functional groups attached to a benzene ring, which includes compounds such as phenol, and toluene. Having biological actions, DNP is used in insecticides, ovicides, acaricides, fungicides, herbicides, some medical therapies, as haptens in some vaccine preparations, and many other products.^{1,2}

Sources:

https://www3.epa.gov/pesticides/chem_search/reg_actions/registration/fs_PC-036000_01-Sep-09.pdf

Known Cross-Reactions:

Clinical Significance:

DNP by itself does not induce an immune response, but it can bind to body proteins and form neo-antigens which can elicit an immune response, resulting in the production of antibodies against both DNP and the human tissue proteins to which it bonded. DNP can change the structure of human proteins, causing them to misfold into a structure similar to amyloid peptide; consequently, the antibodies made against amyloid beta ($A\beta_{42}$) and the antibodies made against DNP bound to human tissue bind to each other and contribute to aggregation.³ Despite its wide use, DNP has been shown to have toxic effects even at low, chronic doses.^{4,5} Usually used in conjunction with other therapeutics, DNP is used for weight loss,⁵ cancer treatment,⁶ and brain disorder therapy.⁷ The list of reported side effects is long and includes rash, fever, sweating, shortness of breath, peripheral neuritis, confusion, agitation, convulsion, coma, agranulocytosis, neutropaenia, and deafness.^{reviewed in 5} Reported deaths due to DNP have risen sharply since 2000.⁵ Extreme hyperthermia usually precedes the death. DNP decreases the formation of high-energy phosphate bonds in mitochondria and at the same time stimulates systemic oxygen consumption; the heat production may lead to uncontrolled hyperthermia.^{reviewed in 5} Physically, DNPs disturb adenosine triphosphate (ATP) production within the cellular mitochondria.⁸ Research findings support the hypothesis that DNPs cancel the ATP formation by hindering/destroying the excited electronic states.² Production of antibody against DNP bound to HSA indicates that the individual cannot metabolize this chemical. This also indicates that DNP as a hapten forms a neoantigen with human tissue, and therefore, antibodies are produced against both DNP and human tissue antigens. In a recent study, it was concluded that because $A\beta_{42}$ antibody reacts strongly with DNP-HSA, the crossing of these antibodies through the barriers may contribute to the pathophysiology of Alzheimer's disease.³

Suggested Reading:

1. Berd et al. Activation markers on T cells infiltrating melanoma metastases after therapy with dinitrophenyl-conjugated vaccine. *Cancer Immunol Immunother*, 1994; 39(3):141-147.
2. Manne et al. TCR rearrangement in lymphocytes infiltrating melanoma metastases after administration of autologous dinitrophenyl-modified vaccine. *J Immunol*, 2002; 169(6):3407-3412.
3. Vojdani and Vojdani. Immunoreactivity of anti- $A\beta$ P-42 specific antibody with toxic chemical food antigens. *J Alzheimers Dis Parkinsonism*, 2018; 8(3):1-11.
4. Dumitras-Hutaru et al. Toxicity of dinitrophenyl derivatives used as pesticides and their environmental impact. *Lucrari Stiintifice*, 2006; 51:29-34.
5. Grundlingh et al. 2,4-Dinitrophenol (DNP): a weight loss agent with significant acute toxicity and risk of death. *J Med Toxicol*, 2011; 7:205-212.
6. Chen et al. Dinitrophenyl hapten with laser immunotherapy for advanced malignant melanoma: a clinical study. *Oncology Letters*, 2017; 13:1425-1431.
7. Kim et al. Nutriproteomics approach to dementia-relevant brain changes. In *Oxidative Stress and Age Related Neurodegeneration*. Y Luo and L Packer (eds.) Taylor & Francis: New York, 2013, pp. 459-480.
8. Drochioiu. Eugen Macovski's concept of biostructure and its current development. In *Life and mind. In search of the physical basis*. S Savva (ed.) Trafford Publ., Canada, USA, Ireland & UK, 2006, pp. 43-60