

2-DEOXY-D GLUCOSE: AN ADJUVANT DRUG USED FOR THE EFFECTIVE TREATMENT OF COVID-19

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ABSTRACT

2-Deoxy D-glucose (2-DG) is used as an anti-Covid drug for moderate to severe cases of Corona virus infection. It is used as an adjuvant drug along with the standard treatment followed for Covid-19. It helps to reduce the supplemental oxygen dependence and thereby hasten the recovery of hospitalized patients and decreases the severity of the infection. The oxygen dependence of Covid-19 patients with 2-DG is reduced by 42% compared to 31% achieved by the standard treatment on Day 3 of infection and treatment. Clinical trials are being conducted to study the Efficacy and Safety of the drug and assessment done by setting various primary and secondary end points to study the improvement in symptoms, risk in mortality and duration of supplemental oxygen.

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INTRODUCTION

The Drug Controller General of India has given approval for emergency use of 2-deoxy D-glucose (2-DG) for treatment of moderate to severe cases of Covid-19 which was developed by Institute of Nuclear Medicine and Allied Sciences, a Lab of Defense Research and Development Organization (DRDO) in collaboration with Dr.Reddy's laboratories, Hyderabad.

This innovative drug is used for treating Covid patients who are struggling for their lives and craving for oxygen amidst the second wave of Corona virus infection. This drug is used as an adjuvant therapy along with the primary treatment. The drug which comes in powdered form in a sachet is taken orally by dissolving it in water.

2-Deoxy-D-glucose is a biochemical molecule which has the hydroxyl group replaced by hydrogen at the 2nd carbon atom of the glucose molecule, so as not to undergo further glycolysis. The basic mechanism of action is that the drug competitively inhibits the production of glucose-6-phosphate from glucose at the Hexokinase enzyme level (step 1) and also at Phospho hexose isomerase level (step 2) of glycolysis required for the breakdown of glucose to yield energy. 2-DG is taken up by the glucose transporters (GLUT) inside the cell^[1,2]. Therefore cells with higher glucose uptake will also have higher uptake of 2-deoxy-D-glucose which hampers viral growth and replication.

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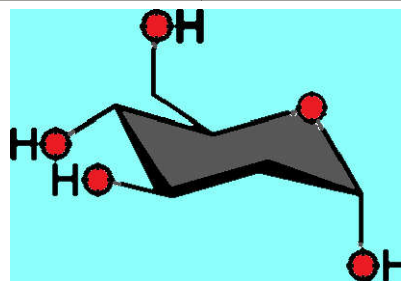


Fig 1 Structure of 2-Deoxy D-Glucose

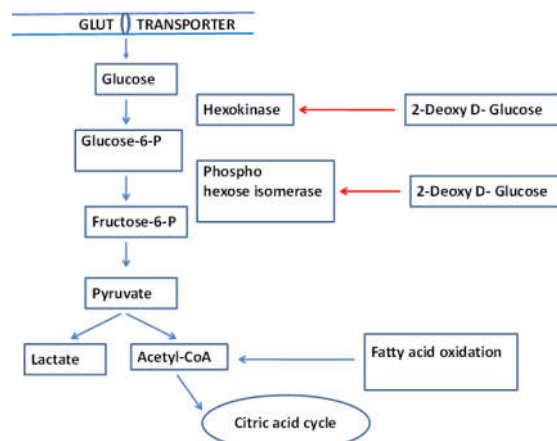


Fig 2 Scheme of 2-DG inhibiting the Hexokinase (step 1) and Phospho hexose isomerase (step 2) enzymes blocking glycolytic pathway. Fatty acids on oxidation enter the metabolic pathway downstream and provides energy in the form of ATP.

The Phase 2 clinical trial was conducted on 110 patients aged 18-65 years over a period of 3 months across 12 sites in India. Those with Covid-19 symptoms like fever, cough, breathlessness, fatigue, body ache, headache, diarrhoea, nasal congestion took part in it. It was reported that phase 2 clinical trial recorded favorable trend as those who received 2-DG returned normal 2.5 days earlier compared to those who didn't receive the drug. The drug was found to be safe in Covid-19 patients and showed significant improvement in their recovery. The trial's primary end point was to measure overall improvement of trial participants on a 10 point clinical progression scale developed by World Health Organization. The secondary end point includes improvement in mortality rates, time dependent on supplemental oxygen, improvement in symptoms etc.

Table 1 WHO clinical progression scale [3]

Score	Description	Condition of the patient
0	No viral load detected	Uninfected
1	Asymptomatic; viral RNA detected	Ambulatory mild disease
2	Symptomatic; independent	
3	Symptomatic; assistance needed	
4	Hospitalised; no oxygen therapy	Hospitalised; mild disease
5	Hospitalized; oxygen by mask or nasal prongs	
6	Hospitalized; oxygen by NIV or high flow	Hospitalized severe disease
7	Intubation and mechanical ventilation	
8	Mechanical ventilation and vasopressors	
9	Mechanical ventilation and vasopressors, dialysis or ECMO	
10	Dead	Dead

Subsequently, phase 3 clinical trials started in January 2021 which will be conducted over a period of 8 months till August 2021 on 220 patients to study the efficacy of the drug. The trials have shown faster recovery of hospitalized patients with Covid-19 along with reduced need for supplemental oxygen. Higher proportion of patients showed negative RT-PCR seroconversion with 2-DG. The drug showed symptomatic improvement and found to be effective in decreasing the oxygen dependence of the patients by 42% versus 31% achieved in standard treatment by day 3. All the available anti-Covid drugs such as Remdesivir, Tocilizumab, Steroids, Ivermectin, Hydroxychloroquine are not yielding good outcomes and steroids exceptionally are being used to combat the inflammatory processes occurring during Covid-19.

2-DG drug which was earlier used as an anti-cancer drug is a glucose analogue which attaches to the virus particle and stops its replication by depleting the available energy supply in the form of glucose. It helps to reduce the further spread of the virus, thereby decreasing the complications and reducing the severity of the infection. High viral load in the body leads to increased oxygen demand and severe infection. This drug inhibits the viral growth and reduces the oxygen dependence and severity of the disease [3]. It selectively gets preferentially and disproportionately accumulated in the inflamed lung tissue that leads to starvation in the lung cells and inhibition of viral replication.

This was studied by the tracing of radio labelled 2-DG drug in the lung tissue [4]. It gets accumulated in the virus infected cells. It is a generic molecule which can be produced in plenty and made available in the Indian market at an affordable price.

Cell culture studies conducted in vitro suggested that cultures in the lab without 2-DG had more viral plaques compared to the ones with 2-DG. The studies were conducted at the center for cellular and molecular biology, Hyderabad [5].

Ministry of defense has published the facts about the emergency approval of the drug in India on 8th May 2021 [5]. Dosage of the drug in phase 3 was increased to 45mg/kg in the morning and 45mg/kg in the evening for a total of 90mg/kg per day [6]. As a single dose of 63 mg/kg/day used for other medical conditions, the drug was found to cause cardiac side effects. 2-DG sachet consists of 2.34 gm of powder and it has to be consumed for 5 to 7 days twice a day for complete cure. It is priced at 990 rupees per sachet.

There is a need for conducting large scale, multi centric, well designed, randomized controlled trial for testing the efficacy and safety of the drug to prove it as an effective treatment against Covid-19 disease.

Acknowledgement

Nil

Conflicts of Interest

There are no conflicts of interest.

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