D-Glucose, in its normal form, is known to most of us. Interestingly, just by replacing an -OH group with a hydrogen, we get 2-deoxy-D-glucose (2-DG) which has excellent medicinal properties. An interesting observation related to glycolysis led to the use of 2-DG as an anticancer drug. Recently, there has been sufficient evidence to support the efficacy of 2-DG as an anti-Covid medication.

Glucose, a simple sugar, consists of six carbon atoms. Aldehyde and alcohol are the two functional groups present in the open chain structure of glucose. Most popularly, glucose is pictured in its open-chain form, although experimentally, it is found that only a negligible amount of the open-chain form of glucose remains in an aqueous solution [1]. Due to a chemical reaction between the aldehyde and one of the alcoholic OH groups present in glucose (circled in Figure 1a), it undergoes a ring formation reaction leading to the formation of α-D-glucopyranose (Figure 1b) and β-D-glucopyranose (Figure 1c). These two isomers only differ in the orientation of the -OH functional group about the star-marked carbon centre as shown in Figures 1b and 1c.

Jean Baptiste Andre Dumas, a French chemist, first coined the name glucose in 1838 for the sugar obtained from honey, grapes, starch and cellulose, although the molecular formula was established 20 years later [2]. Kekulé (in 1866), from polarimetric investigations, found that glucose is dextrorotatory, and hence the molecule was D-glucose. The term ‘D’ stands for dextrorotatory [2]. Thus he proposed the name ‘dextrose’ for this molecule [2]. Glucose is readily available and is generally extracted from its

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Figure 1. Different forms of glucose.

Keywords
Glucose, glucopyranose, 2-DG, anticancer drugs, anti-Covid medication.

Glycolysis is an important metabolic pathway in which glucose is used for the generation of ATP as the main source of energy. Synthetic pathways for the preparation of glucose are uncommon in the literature.

For a long time, 2-deoxy-D-glucose (2-DG) derived from glucose has been investigated for its medicinal activities, especially in anticancer treatment. Here an -OH group at the 2nd position of glucose is replaced by hydrogen, forming the structure shown in Figure 2.

Glycolysis is an important metabolic pathway in which glucose is used for the generation of ATP as the main source of energy, which in turn is utilized for various physiological activities. The phenomenon of an increase in aerobic glycolysis in cancer cells was first described by Otto Warburg in 1930 [3]. He showed that compared to normal cells, malignant cells exhibit significantly elevated glycolytic activity even in the presence of sufficient oxygen and considered this phenomenon the most fundamental metabolic alteration in malignant transformation [3]. This effect is also popularly known as the ‘Warburg effect’. Scientists took advantage of this fact and designed therapeutic strategies that can preferentially kill cancer cells by inhibiting glycolysis [4]. Again, this is possible only because the glycolytic activity of cancer cells is higher than that of normal cells. Any factor that inhibits glycolysis is likely to have a more negative impact on the
survival of cancerous cells compared to that of the normal cell.

2-DG is a competitive inhibitor of the glucose metabolism [5]. Upon transport into the cells, 2-DG is phosphorylated by hexokinase resulting in phosphorylated 2-DG (2-DG-P). However, unlike glucose 6-phosphate (G-6-P), 2-DG-P cannot be further metabolized by phosphohexose isomerase, which converts G-6-P to fructose-6-phosphate, an intermediate in the glycolytic pathway [6]. Inhibition of this rate-limiting step by 2-DG causes a depletion of cellular ATP, leading to blockage of cell cycle progression and cell death in vitro [7]. A clinical trial suggests that 2-DG at doses up to 250 mg/kg appears safe for use in combination with radiation therapy in patients with glioblastoma multiforme [8].

Recently 2-DG has been in the news for its application in Covid-19 treatment in India. On 08 May 2021, the Drugs Controller General of India (DGCI) approved an oral drug based on 2-DG for treating covid patients affected moderately to severely [9]. A leading national newspaper noted that [10] the approval was based on poor evidences. However, a successful in vitro study was done at the Centre for Cellular and Molecular Biology in April 2020, wherein 2-DG exhibited anti-Covid properties, and it led to the necessary permissions for Phase II trials, conducted between May 2020 to October 2020. Phase III trials were also done

**Figure 2.** Cyclic structure of 2-deoxy-D-glucose.

Recently 2-DG has been in the news for its application in Covid-19 treatment in India.
from December 2020 to March 2021. As per the report of the online version of a widely circulated newspaper [11], the drug attaches itself to the virus stopping its multiplication and spreading in the body, thereby controlling the complications and severity it can cause. In other words, the working methodology of the drug remains the same, but, here, the target is different. This drug is currently available for use, and we hope and pray that assistance is given to control the unimaginable situation that has arisen due to the pandemic.

Suggested Reading