





Vol. 6

DIRECTOR GENERAL [DG] AS DEFENSE OF COUNTRY AND DEOXY GLUCOSE [DG] AS FORTIFICATION OF BODY Dr. Badmanaban.R * Principal & Professor ,

Nirmala College of Pharmacy, Muvattupuzha, District-Ernakulam, Kerala-686661, India.Email: badu1977@gmail.com

Abstract:The ability of 2-deoxy-d-glucose (2-DG) to interfere with d-glucose metabolism demonstrates that nutrient and energy deprivation is an efficient tool to suppress SARS CoV-2 cell growth and survival. Acting as a d-glucose mimic, 2-DG inhibits glycolysis due to formation and intracellular accumulation of 2-deoxy-d-glucose-6-phosphate (2-DG6P), inhibiting the function of hexokinase and glucose-6-phosphate isomerase, and inducing cell death. In addition to glycolysis inhibition, other molecular processes are also affected by 2-DG. Attempts to improve 2-DG's drug-like properties, its role as a potential adjuvant for other chemotherapeutics, and novel 2-DG analogues as promising new anti-covid agents are discussed in this review.

Keywords: 2-deoxy-d-glucose, 2-DG analogs, glioblastoma, anticovid therapy

Preamble: Acting as a d-glucose mimic, 2-DG inhibits glycolysis due to formation and intracellular accumulation of 2-deoxy-d-glucose-

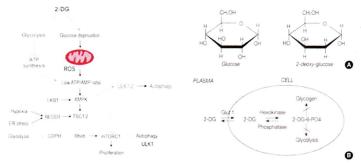


Figure-1: Autophagy in glucose uptake directed by 2-DG

2-Deoxy-d-glucose [CAS: 54-17-6] is a glucose molecule which has the 2-hydroxyl group replaced by hydrogen, so that it cannot undergo further glycolysis. As such; it acts to competitively inhibit the production of glucose-6-phosphate from glucose at the phosphoglucoisomerase level (step 2 of glycolysis). In most cells, glucose hexokinase phosphorylates 2-deoxyglucose, trapping the product 2-deoxyglucose-6-phosphate intracellularly (with exception of liver and kidney); thus, labelled forms of 2deoxyglucose serve as a good marker for tissue glucose uptake and hexokinase activity. Many cancers have elevated glucose uptake and hexokinase levels. 2-Deoxyglucose labelled with tritium or

carbon-14 has been a popular ligand for laboratory research in animal models, where distribution is assessed by tissue-slicing followed by autoradiography, sometimes in tandem with either conventional or electron microscopy.

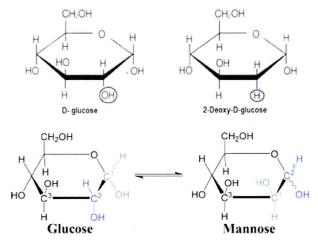


Figure-2: 2-DG & Strucural resemblance with Glucose and Mannose

IUPAC: (4R,5S,6R)-6-(hydroxymethyl)oxane-2,4,5-triol Other names: 2-Deoxyglucose, 2-Deoxy-d-mannose, 2-Deoxy-darabino-hexose, 2-DG

Chemical formula: $C_6H_{12}O_5$, Molar mass : 164.16 g/mol, Melting point: 142 to 144°C (288 to 291°F; 415 to 417 K)

2-DG is uptaken by the glucose transporters of the cell. Therefore, cells with higher glucose uptake, for example tumor cells, have also a higher uptake of 2-DG. Since 2-DG hampers cell growth, its use as a tumor therapeutic has been suggested, and in fact, 2-DG is in clinical trials.^[1-3] A recent clinical trial showed 2-DG can be tolerated at a dose of 63 mg/kg/day, however the observed cardiac side-effects (prolongation of the Q-T interval) at this dose and the fact that a majority of patients' (66%) cancer progressed casts doubt on the feasibility of this reagent for further clinical use.^[4] However, it is not completely clear how 2-DG inhibits cell growth. The fact that glycolysis is inhibited by 2-DG, seems not to be sufficient to explain why 2-DG treated cells stop growing.^[5] Because of its structural similarity to mannose, 2DG has the potential to inhibit Nglycosylation in mammalian cells and other systems, and as such induces ER stress and the Unfolded Protein Response (UPR) pathway.^[6-8]

Clinicians have noted that 2-DG is metabolised in the pentose phosphate pathway in red blood cells at least, although the significance of this for other cell types and for cancer treatment in general is unclear.



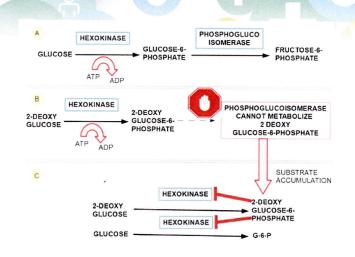


Figure-3: Hexokinase pathway

Work on the ketogenic diet as a treatment for epilepsy have investigated the role of glycolysis in the disease. 2-Deoxyglucose has been proposed by Garriga-Canut et al. as a mimic for the ketogenic diet, and shows great promise as a new anti-epileptic drug.^[9,10] The authors suggest that 2-DG works, in part, by increasing the expression of Brain-derived neurotrophic factor (BDNF), Nerve growth factor (NGF), Arc (protein) (ARC), and Basic fibroblast growth factor (FGF2).^[111] Such uses are complicated by the fact that 2-deoxyglucose does have some toxicity.

A study found that by combining the sugar 2-deoxy-D-glucose (2-DG) with fenofibrate, a compound that has been safely used in humans for more than 40 years to lower cholesterol and triglycerides, an entire tumor could effectively be targeted without the use of toxic chemotherapy.^[12,13]

2-DG has been used as a targeted optical imaging agent for fluorescent in-vivo imaging.^[14,15] In clinical medical imaging (PET scanning), fluorodeoxyglucose is used, where one of the 2-hydrogens of 2-deoxy-D-glucose is replaced with the positron-emitting isotope fluorine-18, which emits paired gamma rays, allowing distribution of the tracer to be imaged by external gamma camera(s). This is increasingly done in tandem with a CT function which is part of the same PET/CT machine, to allow better localization of small-volume tissue glucose-uptake differences.

On May 8, 2021, the Drugs Controller General of India approved an anti-COVID oral drug, developed by DRDO, for emergency use as adjunct therapy in moderate to severe coronavirus patients based on this compound. The drug comes in powder form in sachet, which is taken orally by dissolving it in water. Clinical trial results have shown that 2-DG helps in faster recovery of hospitalised patients and reduces supplemental oxygen dependence.^[16]

Resistance to 2-DG has been reported in HeLa cells and in yeast; in the latter, it involves the detoxification of a metabolite derived from 2-DG (2DG-6-phosphate) by a phosphatase.^[8,17,18] Despite the existence of such a phosphatase in human (named HDHD1A) However it is unclear whether it contributes to the resistance of human cells to 2DG or affects FDG-based imaging.

The present invention provides a process for the synthesis of 2deoxy-D-glucose comprising haloalkoxylation of R-D-Glucal wherein R is selected from H and 3, 4, 6-tri-O-benzyl, to obtain alkyl 2-deoxy-2-halo-R- α/β -D-gluco/ mannopyranoside, converting alkyl 2-deoxy-2-halo-R- α/β -D-gluco/mannopyranoside by reduction to alkyl 2-deoxy- α/β -D-glucopyranoside, hydrolysing alkyl 2-deoxy- α/β -D-glucopyranoside to 2-deoxy-D-glucose.^[19] Scheme of synthesis:

The preferred synthetic reactions and conditions for each individual steps of the above process are set forth below.

The reaction scheme for the reactions involved in the process of the invention are also given below:

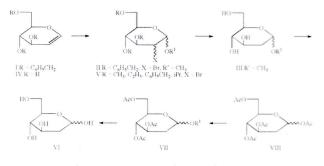


Figure-4: 2-DG synthetic scheme

The present invention provides a process for the synthesis of 2deoxy-D-glucose comprising haloalkoxylation of R-D-Glucal wherein R is selected from H and 3, 4, 6-tri-O-benzyl, to obtain alkyl 2-deoxy-2-halo-R- α/β -D-gluco/mannopyranoside, converting alkyl 2-deoxy-2-halo-R- α/β -D-gluco/mannopyranoside by reduction to alkyl 2-deoxy- α/β -D-glucopyranoside, hydrolysing alkyl 2-deoxy- α/β -D-glucopyranoside to 2-deoxy-D-glucose.^[19]

Scheme of synthesis:

2

The preferred synthetic reactions and conditions for each individual steps of the above process are set forth below.

The reaction scheme for the reactions involved in the process of the invention are also given below:

Innovative approach: The present invention relates to a process for the synthesis of 2-deoxy-D-glucose.

Background:2-deoxy-D-glucose is useful in control of respiratory infections and for application as an antiviral agent for treatment of human genital herpes.Prior art for preparation of 2-deoxy-D-glucose while operable, tend to be expensive and time consuming.

Objects: The main object of the present invention is to provide a process for the synthesis of 2-deoxy-D-glucose resulting in good yield and with good purity. Another object of the invention is to provide an economical process for the synthesis of 2-deoxy-D-glucose.

Summary: A process that would produce 2-deoxy-D-glucose economically and with desired purity, is a welcome contribution to the art. This invention fulfilsthis need efficiently.

Accordingly, the present invention relates to a process for the synthesis of 2-deoxy-D-glucose comprising haloalkoxylation of R-D-glucal wherein R is selected from H and 3,4,6-tri-O-benzyl, to obtain alkyl 2-deoxy-2-halo-R- α/β -D-gluco/mannopyranoside, converting alkyl 2-deoxy-2-halo-R- α/β -D-gluco/mannopyranoside by reduction to alkyl 2-deoxy- α/β -D-glucopyranoside, hydrolysing alkyl 2-deoxy- α/β -D-glucopyranoside to 2-deoxy-D-glucose.^[20-25]

In one embodiment of the invention, the alkyl 2-deoxy- $\alpha/\beta\text{-D-glucopyranoside}$ is obtained by

(a) haloalkoxylating 3,4,6, tri-O-benzyl-D-glucal to alkyl 2-deoxy-2-halo-3,4,6-tri-O-benzyl- α/β -D-gluco-/mannopyranoside,

(b) subjecting alkyl 2-deoxy-2-halo-3,4,6-tri-O-benzyl- α/β -D-gluco/mannopyranoside to reductive dehalogenation and debenzylation to obtain alkyl 2-deoxy- α/β -D-glucopyranoside.

In another embodiment of the invention, in step (a) haloalkoxylation of 3,4,6-tri-O-benzyl-D-glucal is carried out by reaction with a haloalkoxylating agent selected from a N-halosuccinimide and a N-haloacetamide, and alcohol.

In another embodiment of the invention, alkyl 2-deoxy- $\alpha/\beta\text{-}D\text{-}$ glucopyranoside is obtained by

(a) haloalkoxylating D-glucal to alkyl 2-deoxy-2-halo- α/β -D-gluco/mannopyranoside;

(b) subjecting alkyl 2-deoxy-2-halo- α/β -D-gluco/ mannopyranoside to reductive dehalogenation and hydrogenation to obtain alkyl 2-deoxy- α/β -D-glucopyranoside.

Converting 3,4,6-tri-O-benzyl-D-glucal (I) to alkyl 2-deoxy-2-halo-3,4,6-tri-O-benzyl- α/β -D-gluco-/mannopyranoside (II).

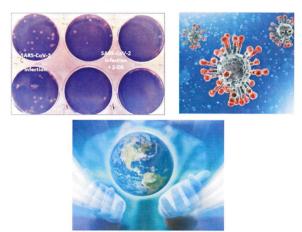
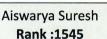


Figure-5: Serological culture of SARS-CoV-2 with 2-DG

GPAT WINNERS







Aswathy Surendrar Rank:2137

RESOURCE PERSONS DETAILS:

Dr. Fels Saju



- 1. TOPIC:Entreprenership in pharmacy education ,Organised By: Alshifa College Of Pharmacy, Date: 29/04/2021
- Topic: Fine Tune your Pharmacy Career ,Organised By: Al Azhar College Of Pharmacy, Thodupuzha, Date: 26/03/2021

Conclusion: With the country battling the second wave of Covid-19 infections, The Drugs Controller General of India (DCGI) on Saturday [8th May 2021] approved a drug developed by the DRDO for emergency use. The drug: 2deoxy-D-glucose (2-DG) - has been approved as an adjunct therapy in moderate to severe cases of coronavirus.Clinical trial results have shown that this molecule helps in faster recovery of hospitalized patients and reduces supplemental oxygen dependence, an official of the Defence Research and Development Organisation (DRDO) was quoted as saying.According to the official statement, "clinical trial results have shown that this molecule helps in faster recovery of hospitalised patients and reduces supplemental oxygen dependence.""Higher proportion of patients treated with 2-DG showed RT-PCR negative conversion in COVID patients. The drug will be of immense benefit to the people suffering from Covid-19," the statement goes on to say. The 2-DG drug, which comes in powder form in sachets, has to be taken orally by dissolving it in water. It accumulates in the virus infected cells and prevents virus growth by stopping viral synthesis and energy production," said the official statement by the Government of India. The DRDO says that the 2-deoxy-D-glucose (2-DG) drug can easily be produced and made available in plenty in the country since it is a generic molecule and analogue of glucose.

- Univeiling CHIP: The New Age Budiness Strategy, OrganisedBy: Junior Chamber International, Kottayam, 24/03/2021
- Aware and Beware ; Responsible usage of medicines, Organised By: Junior Chamber International , Karmugal, Date:23/03/2021

Dr. Badmanaban R



MIK

- Topic: Outcomes based education system for pharmacy, Organised By: School of pharmacy,Techno university , Kolkata, Date: 19/12/2020
- 2. Topic: Marker based standardization and quality control,OrganisedBy: School of Pharmacy, Techno University Kolkata, Date:9/08/2020

GRADUATION CEREMONY



The graduation ceremony of pharm-D (2014-2020) batch students was conducted ceremoniously. The inaugural address was delivered by Administrator Rev.Fr.Jos Mathai Mailadiath, Principal Dr.Badmanaban R gave the graduation day speech.



INTERNATIONAL CONFERENCE ON INNOVATIONS IN DEVELOPING PHYTOPHARMACEUTICALS FROM INDIGENOUS MEDICINE."

In "Nirmala College of Pharmacy, Department of Pharmacognosy organised a webinar entitled "International Conference on Innovations in Developing Phytopharmaceuticals from Indigenous Medicine." as 12 thModule of NILA (Nirmala Ignites Learning Aspiration). The main aim of the seminar is to create awareness on the regulations and possible innovations and scope of



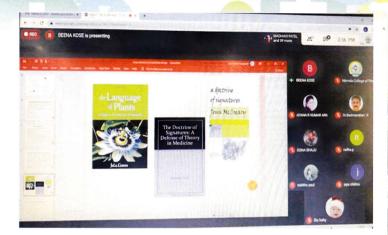
clinically proven phytopharma-ceuticals for betterment of health of society.

The first session was on the Topic: "Moving from Traditional Research to Innovative Natural Products for Sustainable Future and Development."led by Dr.Mahendran Sekar (Associate Professor, Faculty of Pharmacy and Health Sciences, University Kuala Lumpur Royal College of Medicine Perak, Malaysia).



The second session was on the Topic: "Phytopharmaceutical Regulations in India-Scope for New Drug Development"led by Dr.VivekanandanKalaiselvan(Principal Scientific Officer, Indian Pharmacopoeial Commission, Ghaziabad, Uttar Pradesh.)The third session was on the Topic: "Nature's Clues in Drug Discovery" led by Dr. Beena Briget Kuriakose (Assistant Professor, College of Applied Sciences, King Khalid University, Kingdom of Saudi Arabia). In the webinar about 100 participants from different institutions were benefited and was very informative and useful.



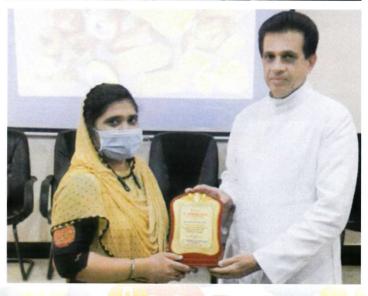


NUTRITION AMONG YOUTH

The awareness program conducted by NSS unit on the topic "Nutrition among youth".







PIPE COMPOSTING IN HOUSES OF AVOLYPANCHAYATH







NSS unit of Nirmala College of pharmacy, have provided free pipe composts over twelve houses of avoly panchayat.

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Entrepreneurship Awareness Program

The entrepreneurship awareness program organised in association with District Industries centre, Ernakulam. Resource Persons : Mr.V. Anilkumar, Ms. PNamitha, Taluk Industries Officers Ms.Priya Paul, Taluk Industry development officer



NEAR TO REAL EXPERIENCE AND DISCUSSION ON PHARMACEUTICAL INDUSTRY

Resource person: Mr.Aghil M Joy, Manufacturing Director , Clans Life care, Kochi.





DETAILS OF WORKSHOPS/SEMINAR/GUEST LECTURE CONDUCTED (JULY 2020-JUNE 2021)

SL	DATE	TOPIC	SPEAKER	Seminar/ Workshop
1	11/7/20	Statistical software training program	Dr. Muralidhara Anandamurthy (Member, JMP global academic)	Webinar
2	22/07/20	Patient-centric drug information by reducing medication errors	Mr. VikasArora & Ms. Sheena Chugh	Webinar
3	04/08/20	Pharma graduate to a scientist-an expedition"	Dr. Anish C.K. (Principal Scientist and team lead, Jansen Vaccines, Netherlands)	Webinar
4	17/08/20	"Facts of Human brain : Rewards and Memory"	Dr.Arulmozhi S (HOD Department of Pharmacology, Pune College of Pharmacy	Webinar
5	22/08/20	Drug reposition: transformation of hardwork into smart work	Dr.Bijo Mathew, M Pharm, PhD, Division of Drug Design & Chemistry Research Lab, Associate Professor ,Ahalia School of Pharmacy, Palakkad	Webinar
6	22-28 th / 08/2020	Applications of computational clinical bio-pharmaceutics in pharmaceutical product development	DR.RAJKUMAR M ,Deputy General , Clinical Research, USV Pvt.Ltd Mumbai DR.K.GOWTHAMARAJAN M. Pharm, PhD Professor and head of Department of pharmaceutics J.S.S. College of Pharmacy, Ooty, TN, India	International Conference

SL	DATE	ΤΟΡΙϹ	SPEAKER	Seminar/ Wor
			Dr.VVSNarayana Reddy Kari,M. Pharm, PhD Professor and head of Department of pharmaceutics J.S.S. College of Pharmacy, Ooty, TN, India DR. M.K. UNNIKRISHNAN M. Pharm, PhD Principal National college of pharmacy Kozhikode, Kerala, India DR.DIXON THOMAS Associate Professor & Chair Department of Pharmacy Practice College of Pharmacy, Gulf Medical University DR. SHYAM SUNDER V PANCHOLI Former professor College of Pharmacy, Jazan, Kingdom of Saudi Arabia	
7	18/09/20	" MOODLE A PLATFORM FOR ONLINE EDUCATION''	Dr.Shaji George, Professor and Head of Pharmacy Practice department, Nirmala College of Pharmacy	FDP
8	18/9/20	"International Conference on Innovations in Developing Phytopharmaceuticals from Indigenous Medicine."	 Dr. VivekanandanKalaiselvan Principal Scientific Officer Indian PharmacopoeialCommision, Ghaziabad, Uttar Pradesh. Dr. MahendranSekar Associate Professor, Faculty of Pharmacy and Health Sciences University Kuala Lumpur Royal College of Medicine Perak, Malaysia. Dr. BeenaBrigetKuriakose Assistant Professor College of Applied Sciences King Khalid University Kingdom of Saudi Arabia 	International Webinar
9	2-10-2020 & 3-10-2020	"Intraveneous medication safety and role of practicing pharmacist"	Dr. Manjula Devi A S, Associate Professor, SRIPS, Coimbatore.	International Webinar
10	17/10/2020	"Maintenance and Calibration of Laboratory Equipments"	Mr. Shajan P J ,Technical Officer, VJCET, Vazhakulam	Training progran
11	29/10/2020	"MOODLE A PLATFORM FOR ONLINE EDUCATION"	Dr.Fels Saju, Assistant Professor, Pharmaceutics Department, Nirmala College of Pharmacy	FDP
12	30/12/20	"Importance of regulatory affairs in pharmacy and medical devices"	Mr. Ravi Krishnan, Technical Manager, Quality Assurance and Regulatory Affairs, Wipro Ltd., Bangalore	Invited talk
13	08/02/21	Workshop On "In Silico Drug Design Using Autodock"	Dr. Prasanth Francis, AssistantProfessor, Pharmaceutical Chemistry department, Nirmala College of Pharmacy	Hands on trainin
14	19/02/21	A Near To Real Experience And Discussion On Pharmaceutical Industry	Mr. Aghil M Joy, Manufacturing Director/Partner, Clans Life care,Kochi.	Invited talk
15	23/2/21	Micromedex Drug Information Software	Dr.Merin Joseph ,Assistant professor, Pharmacy Practice department ,Nirmala College of Pharmacy	Hands on trainin

SL	DATE	ΤΟΡΙϹ	SPEAKER	Seminar/ Workshop
16	03/03/21	Menstrual health and hygiene	Ms.Kavya R Menon, Eco-Feminist ,Consultant –Gender and environment	Invited talk
17	10/03/21	Add –on course on essential management skills for career development	Mr.JaisonArackal, Director and Chief Trainer, Success Mine Training	Personality development program
18	23/5/21	Systematic Review and Meta -Analysis	Mr. Muhammed Rashid ,DST INSPIRE Fellow, Research Scholar ,MCOPS,MAHE	Online workshop and hands on training
19	27/5/21	HPTLC : Technique and pharma applications	Ms.Sneha Singh, Application specialist, ANCHROM	Webinar
20	29/05/21	Preparation for a career in regulatory affairs	Dr.AnjithaJoy,Consultant regulatory specialist RRDM,GSK	Webinar

Day Celebration- 2020 25/08/2020

National Pharmacy week Celebration 2020

21/11/2020



All India Pharmacy Quiz Preliminary 2020



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CHRISTMAS CELEBRATION fab-Yule-Us 2020



World Pharmacist Day 25/09/2020













World cancer day 04/02/2021



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Ms. Niya Mariya **Research Associate Trainee** Wissen Infotech, Bangalore Rs. 3,61,500/- per annum

Centralized Monitoring Assistant, IQVIA, Kochi Rs.3,13,200/- per annum



ol Shai Intern-Patient Advocate International AutoCatal Safety Science Analyst, Clinical Pharmacist Clinical Pharmacist Pavya Technologies Pvt. Ltd. Pharma Lasf India Pvt. Ltd., Bangalore Apolla Adlux Hospital, Kochi Shenoy's Care Pvt. Ltd., Kochi Rs.2.16,000/. per annum Rs. 32,65,727 / per annum Rs.2.00,000/. per annum Rs.2.76,000/. per annum Rs. 3,28,572/- per annum



11



Mr. Sanio Saijan **Clinical Pharmacist** Rs 2,00,000/- per annum Rs.2,76,000/- per annum





Ms. Swapna Saiu **Research Associate Trainee** Wissen Infotech, Bangalore Rs. 3,61,500/- per annum

Rs.3.61.500/- ner annum



Pharmacy Trainer Central Govt. Project(DDU-GKY) Delwin Formulations, Peerimedu Rs. 1,80,000/- per annum







Ms. Saniana Charley Safety Science Analyst,

Mr. Stelvin Antony **Clinical Pharmacist**

Congratulations.... PLACEMENTS





Afna Azeez







Agnes Mathew





Anitta C Jaison Ann Aswathy Thomas



Teresa Cyriac



Bella Baby

PUR HEAVENLY PATRON

Jashna K Kani

Sahila T S





Dr.Merrin Joseph Assistant Professor Department of Pharmacy Practice



Ms. Sonia Assistant Professor Department of Pharmaceutics

Nirmala College of Pharmacy Muvattupuzha

Affiliated to Kerala University of Health Sciences, Thrissur Tel: 0485 2836888, 2830666, 9447292536 E-mail: nip mvpa@yahoo.co.in

COURSES : **B.**Pharm (Batchelor of Pharmacy - 4 yrs) M.Pharm in Pharmaceutics (2 yrs) Pharm.D (Doctor of Pharmacy - 6 yrs)