

# GreenDiol

Made in and from Nature (The Greenest), for Humans and Nature (Multi-Beneficial Functions)

- I. Company introduction
- II. 2,3-Butanediol from Nature
- III. 2,3-Butanediol manufactured by GS Caltex
- IV. GS Caltex GreenDiol



# **I.** Company Introduction





Grow Sustainably GS Group is leading the change for a sustainable future

- Total assets: US\$ 63 bil.
- Sales: US\$ 72 bil.
- Employees: 33,000

- Overseas presence: 32 Countries
- Overseas corporations and branches: 93 Global Sites
- Subsidiaries: 67 ('22)

#### **Business Area**

Energy & Power					Retail &	Trading	Construction & Service	
<b>GS</b> Energy	<b>GS</b> Caltex	<b>GS</b> Power	GS E&R	GS EPS	SRetail	<b>GS</b> Global	S E&C	<b>GS</b> Sports
• Power E&P	<ul> <li>Petroleum</li> <li>Petrochemicals</li> <li>Base oil</li> <li>Lubricants</li> <li>Gas stations</li> </ul>	<ul> <li>Electric Power District heating</li> <li>&amp; Cooling Renewable Energy</li> </ul>	Combined heat & power     Coal-fired Renewable Energy	<ul> <li>Electricity</li> <li>Power Plant</li> <li>Bio-mass</li> <li>Wind power</li> <li>Fuel cell power</li> </ul>	<ul> <li>Convenience store</li> <li>Supermarket</li> <li>TV &amp; Mobile shopping</li> </ul>	International Trading	<ul><li>Plant</li><li>Construction</li><li>Infrastructure</li></ul>	<ul> <li>FC Seoul football</li> <li>Seoul Kixx volleyball</li> </ul>



**GS** Caltex Leading energy and chemical enterprise in the global market

#### **Business Area**



Revenue	US\$ 58.5 bil. ('22)		
Operating Income	US\$ 4.0 bil. ('22)		
Employees	~3,200 persons		



Refining	(World's 4 <sup>th</sup> largest)
Heavy Oil Upgrade	275,000 BD (No.1 in Korea)
Base Oil	26,000 BD



Aromatics	2,800 KT/yr
Ethylene	750 <b>KT/yr</b>
Polyethylene	500 KT/yr
Polypropylene	180 KT/yr

To be the most respected energy & chemical company through Business, Digital & Green Transformation



**Green Transformation** through 4 sectors Biochemicals with diols (2,3-BDO, 1,3-PDO) & acids (3-HP)

#### **Green Transformation Area**

#### Biofuel

By producing biofuels from biomass, a sustainable feedstock, we contribute to reducing greenhouse gas emissions by replacing products produced from conventional fossil fuels



- Bio Jet Fuel • Bio Marine Oil
- Bio Diesel

#### H<sub>2</sub>,CCUS

Expanding our hydrogen business in line with the trend of revitalizing the hydrogen economy and low-carbon policies



- Producing low carbon hydrogen
- Pre-occupying demand (mobility/fuel cell business)
- Building the CCUS infrastructure

#### Lower Carbon Business

### **Biochemical**

Developing technologies to produce various biochemicals used in cosmetics, agriculture, and plastics through eco-friendly processes

- Bio Diols (2,3-BDO, 1,3-PDO)
- 3-Hydroxypropionic acid



#### **Plastic Recycle**

Since 2010, we have been conducting a circular business to recycle waste plastics into petrochemical raw materials and products through mechanical and chemical recycling

Chemical Recycle
Mechanical Recycle



Green Transformation with Biofuel, H<sub>2</sub>/CCUS, Plastic Recycle & **Biochemical** 



### White Bio Global Standard Builder

Achieving the GS Caltex Goal and its Lower Carbon Vision

#### White Bio Development Center **BioTechnology Team BioProcess Team** Bio Demo Plant Team **BioSolution Team Diols PJT Team** Biocatalyst & Process Development **Demo Plant Operation** Strategy & Business Commercialization Fermentation Tech. & Scale-up engineering & Verification development Development Lab Downstream • Market analysis Technical capacity • Biz. Model Microbes availability for the Pilot Validation Market development • Techno-Economic Lab. Fermentation commercial scale Analysis Optimization • O/I Partnership Scale-up Design Prototype production • Basic design PKG (for marketing)

#### Organization

#### **Areas**

Cosmetics & Personal care	Agriculture	Food & Beverages	Industrials
	Agriculture		magstrais

White Bio Development Center was established in 2022 & ~100 members are working for Industrial Biotechnology



GS Caltex World's leading infrastructures White Bio has started since 2006

Infrastructure

#### **History**

- Start of GS Caltex's WhiteBio (2006)
  - Start of Biobutanol R&D
- Start of 2,3-BDO R&D (2009) 3
- GS Bio Establishment (2010) 3
- Pilot plant (2010 ~ Present)
  - Biobutanol (2010~2015)
  - 2,3-BDO (2013~2014)
- Gunsan Demo plant (2015 ~ Present)
  - Plant design & Construction (2015~2019)
  - Operation (2019~Present)
- Yeosu Demo plant (2016 ~ Present)
  - Plant design & Construction (2016~2017)
  - Commissioning & prototype production (2018)
- Start of 3-HP R&D (2021 ~ Present) 3
- Open Innovation (2021~ Present)
  - Collaboration with partners (~ Present)











GS Caltex has developed the modest and standardized Bio Demonstration Plant



# II. 2,3-Butanediol from Nature

There is a reason for everything that exists in universe

### **2,3-Butanediol from Nature**



#### 2,3-BDO has been found in humans, animals, and insects. It also exists in foods, animal feedstocks, and soil.

Human Body	• Human	Body	2-20 uM	Human Metabolome Database (http://www.hmdb.ca/metabolites/HMDB03156)
		Sheep Rabbit	Detected	Canadian Journal of Animal Science (1981) 61:649-656 The Biochemical Journal (1954) 57: 177-180
		Cat	Detected	The Biochemical Journal (1954) 57: 177-180
Livestock	• Animals	Fish	0.006 mg/kg	The EFSA Journal (2004) 166
		Livestock feeds	0.5-24 g/kg	Canadian Journal of Animal Science (1981) 61:649-656 Journal of the Science of Food and Agriculture (1973) 24: 613 -648.
	Insects	Bee	Detected	Journal of apicultural science (2006) 50(2):115-126 Evidence-Based Compl and Alter Med (2009) 6(1):113-121
			~ 2,900 mg/kg	The EFSA Journal (2004) 166
Bees, honey		Wine	527.9 µg/L	Molecules (2010) 15 : 9184-9196
OH & propolis			1,200 µg/L	Eur Food Res Technol (2008) 227:287-292
		Vinegar	~ 850 mg/kg	The EFSA Journal (2004) 166
CH <sub>3</sub>	<ul> <li>Foods &amp; Beverages</li> </ul>	Cheddar cheese	~ 90 mg/kg	The EFSA Journal (2004) 166
H <sub>3</sub> C		Beer	50 ~ 150 mg/L	Beer Composition and Properties, Beer in Health and Disease Prevention (2008) 222
ОН		Makgeolli (Rice wine)	Detected	Molecules (2013) 18:5317-5325
Foods		Fermented Pastes	Detected	Food Engineering Progress (2014) 18(3):248-255 Food Engineering Progress (2014) 18(4):300-306 Korean Journal of Food Preservation (2017) 24(2):187-195
		Kimchi	Probability	Journal of microbiology and biotechnology (1997) 7(1):68-74
		Fermented Beef jerky	2.79%	Polish Journal of Food and Nutrition Sciences (2016) 66(1):25–30
Beverages		Raspberry	~ 2.3 mg/kg	The EFSA Journal (2004) 166
		Coconut oil	Detected	Journal of Food Science (2015) 80(1):49-54
		Propolis, Honey	~ 52.05%	Inter J of Pharma and Bio Sciences (2015) 6(2):374-380 Zeitschrift für Naturforschung C (2002) 57:395-402
Soil	• Soil		Detected	Plant, Cell and Environment (2014) 37:813–826

### For Humans

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#### 2,3-BDO has positive effects on human body.

#### Detoxifying agent in liver, Boosting immunity, Treating inflammation.

THE JOURNAL OF BIOLOGICAL CHEMINTRY  $\oplus$  1993 by The American Society for Biochemistry and Molecular Biology, Inc.

Vol. 268, No. 27, Issue of September 25, pp. 20185-20190, 1993 Printed in U.S.A.

#### Metabolism of 2,3-Butanediol Stereoisomers in the Perfused Rat Liver\*

(Received for publication, February 16, 1993, and in revised form, June 2, 1993)

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The identification of 2.3-butanediol in sera of alcoholics led to the hypothesis that it may be a specific marker of alcohol abuse. We have investigated the metabolism of the individual isomers of 2,3-butanedio (2R,3R-, 2S,3S-, meso-2,3-butanediol and racemic 2.3-butanediol) in perfused livers from fed rats. Rates of uptake of the isomers decrease in the order (i) 2R,3R-, (ii) meso-, (iii) 2S,3S-2,3-butanediol. We observed interconversion of isomers and oxidation to acetoin with 2R, 3R- and meso- but not with 2S, 3S-2,3-butanediol. In perfusions conducted in deuterium oxide, interconversion of isomers was accompanied by incorporation of deuterium. Thus, interconversion of isomers occurs via a reversible oxidation to acetoin with incorporation of hydrogen from water. In perfu-sions with either 2R,3R- or meso-[2-14C]2,3-butanediol, the substrates were converted to labeled acetate R-3-hydroxybutyrate and CO<sub>2</sub>, suggesting that 2,3-butanediol is oxidized to acetyl-CoA via acetoin.

Although the epidemiology of some cases of alcoholism suggests a genetic predisposition, to date there are few, if any, reliable tests to identify susceptible individuals (1, 2). Positive identification of both prealcoholic and alcoholic tendencies would benefit from the availability of biochemical markers (3, Reports of elevated 2,3-butanediol (butanediol)<sup>1</sup> in the serum and urine from inebriated alcoholics suggest that this compound could be of diagnostic value (5-8). It has been proposed that the plasma concentration of butanediol could be used as a marker of ethanol abuse and as an index of compliance with treatment of alcoholism (1).

2,3-Butanediol is formed in mammalian cells (9-17) and in microorganisms (18-22) by the reduction of acetoin (3-hydroxybutan-2-one), a minor metabolite of pyruvate (23-31). In mammals, acetoin is formed by a side reaction of pyruvate dehydrogenase (23), as illustrated in Fig. 1, whereby hydroxy- MS assay for butanediol, we demonstrated that both diaster-

2,3-butanediol serves as a



FIG. 1. Pyruvate dehydrogenase-mediated synthesis of ace-toin. TPP and HETPP, thismine pyrophosphate and hydroxyethyl thiamine pyrophosphate, respectively, are both bound to pyruvate dehydrogenase (PDH). The dotted line represents the normal transfer from hydroxyethylthiamine to lipoamide through the E<sub>0</sub> subunit of the pyruvate dehydrogenase complex

denses with acetaldehyde (derived mostly from ethanol oxidation). We have recently shown the general nature of acyloin (3-hydroxyalkan-2-one) formation by demonstrating that pyruvate dehydrogenase catalyzes the condensation of short to medium chain saturated aldehydes with hydroxyethylthia mine pyrophosphate to form the corresponding Cn+2 acyloins (32)

The mammalian metabolism of butanediol (23-27) is not as well documented as that in microorganisms (18-22). Two asymmetric carbon centers in butanediol give rise to three possible isomers, 2R.3R- (RR), 2S.3S- (SS), and R.S- (meso) butanediol. The first two are enantiomers, and the third is a meso form. Plasma and urine samples from alcoholics were extracted, derivatized with achiral reagents, and analyzed by either gas chromatography-mass spectrometry (GC-MS) (5, 8) or gas chromatography (GC) (6, 33). Two peaks were identified as the meso-isomer and a coeluting mixture of the RR- and SS-butanediol enantiomers in unknown proportions.

It has been suggested that this latter peak is more specific to alcoholism (6) as it remains elevated in sera from abstinent alcoholics with liver cirrhosis (34, 35). Using a sensitive GC-

### **Channeling Metabolism**

detoxifying product in liver

#### Activation of NK cell cytotoxicity by the natural compound 2,3-butanediol

Hsin-Chih Lai,\*<sup>1</sup> Chih-Jung Chang,<sup>2</sup> Chun-Hung Yang,\*<sup>5</sup> Ya-Jing Hsu,\* Chang-Chieh Chen,\* Chuan-Sheng Lin,\* Yu-Huan Tsai,\* Tsung-Teng Huang,\*<sup>1</sup> David M. Ojcius,<sup>1,3</sup> Ying-Huang Tsai,\* and Chia-Chen Lu<sup>#,1</sup>

<sup>1</sup>Deparament of Medical Biosechology and Lanony Science, Yosen for Parlogenia Riceria and Center for Molecular and Clinical Biomenology, "Deparament of Mortbiology and Biomunology, College of Medicine, Dang Gang University, Tokan, Quantum Coll., "More and Apple of Clinical Yealth Sciences Research Insuiture, Control of Agriculture, Taiwan, Republic of Clinica, Yealth Sciences Research Insuiture, Control of Agriculture, Taiwan, Republic of Clinica, West, Uliver, State and Sciences Research Insuiture, Control of Agriculture, Taiwan, Republic of Clinica, Yealth Sciences Research Insuiture, Canada Gang Munoral Hospital, University of Clanican, Taiwan, Republic of Clinica, Parl Clinica, Parl Marcel Hospital, University Taiwan, Bergalistic Clinica, Parl Marcel, Clinica, Clinica, Clinica, Clinica, Sciences, Parl Catholic University Taiwan, Bergalistic Clinica, Sciences Research Institute, Cathog of Medicine, Faler Catholic University Taiwan, Bergalistic Clinican, Uliversity and Clinican, Sciences Research Berganization, Clinican, Clinican, Clinican, Clinican, Sciences, Parl Catholic University, Taiwan, Bergalistic Clinican, Uliversity and Clinican, Lanon Sciences Research Institute, Clinican, Clinica

RECEIVED JANUARY 19, 2012; REVISED JUNE 7, 2012; ACCEPTED JUNE 29, 2012. DOI: 10.1189/jb.0112924

#### ABSTRACT

The natural compound 2.3-BTD has diverse physiological effects in a range of organisms, including acting as a detoxifying product of liver alcohol metabolism in humans and ameliorating endotoxin-induced acute lung injury in rats. In this study, we reveal that 2,3-BTD enhances NK cell cytotoxic activity in human pNK cells and NK92 cells. Treatment of NK cells with 2,3-BTD increased perforin expression in a dose-dependent manr. This was accompanied by elevated JNK and ERK1/2 MAPK activities and enhanced expression of NKG2D/ NCRs, upstream signaling molecules of the MAPK pathways. The 2,3-BTD effect was inhibited by pretreatment with inhibitors of JNK (SP) or ERK1/2 (PD) or by depleting NKG2D/NCRs or JNK1 or ERK2 with siRNA. These result indicate that 2,3-BTD activates NK cell cytotoxicity by NKG2D/NCR pathways and represent the first report of the 2,3-BTD effect on activation of innate immunity cells. I Leukoc Biol 92: 807-814: 2012.

#### Introduction

The low molecular-weight compound 2.3-BTD, which is widely synthesized in humans [1], yeast [2], and bacteria [3], is involved in a variety of biological activities. These include homeostasis of al oH when hacieria grow to high cell density [4]

[10]. We also characterized the effect of RSV on NK cell NKG2D/ NCR signaling and cytotoxic activity [11]. However, whether 2,3-BTD plays a role in modulating immune activity via regulation o NK cell cucroxicity activity remains to be characterized. The NK cells are important for early host defense against infection and tumors [12-14]. NK cells are with the capability of granule exocytosis by releasing granule proteins, such as perforin, granzymes, and granulysin [15]. The NK cell cytotoxic activity is controlled by coordinated signals generate from the ligation of inhibitory and activating receptors [16]. The major activating receptors are the NCRs, comprising con

[8], and potent CNS-depressant effect in rats [9]. This remarkable

functional repenoire suggests that 2.3-BTD may act as a signaling

molecule in a wide variety of species [6, 8]. Recently, we reported

that 2,3 BTD ameliorates endotoxin-induced acute lung injury in rats

duced NKp44 [19]. Moreover, the NKG2D receptor, which is also identified in human T cells [20], also involves activating NK cell cytotoxicity [21]. The ligation of the activating receptors lead to activation of a cascade of intracellular signaling, resulting in polarization and exocytosis of granules to lyse the TS [16, 22]. In NK cells, ERK, JNK, and p38 are intermediates of the important signaling MAPK pathways that regulate gran-

tion which is **Boosting Immune System** 

2,3-butanediol enhances immunity by activating innate immunity cells



Keywords: 2.3-butanediol: LPS: NF-xB: Acute lung injury: Inflammation

#### 1. Introduction

The capacity for production of the low-molecular-weight hydrocarbon, 2.3-butanediol, from pyruvate has been widely identified in different bacterial species, including all species of Serratia and Enterobacter, as well as some species of Klebsiella, Erwinia, Bacillus and Aeromonas [1], Previous studies

densities, regulation of the cellular NAD/NADH ratio in bac teria [2], an agent for storage of organs such as the liver [1], a biomarker for yeast strain differentiation [3], and a plasma biomarker of ethanol abuse and an index of compliance in alcoholism treatment [4]. The derivatives of 2,3-butanediol, including liquid fuel additives, anti-freeze agents, food flavor ings, solvents and plastics, are also widely used in industry [1].

**Controlling Inflammation** 2,3-butanediol ameliorates endotoxin-induced lung injury

Article

# stitutively expressed NKp46 [17] and NKp30 [18], and the in-

### **For Humans**

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H<sub>2</sub>C

A patent about the usage of 2,3-BDO in treatment or prevention of obesity, insulin resistance, and diabetes and in the reduction of metabolic ageing has been issued ('21).

2,3-BDO treatment has shown good biocompatibility and durability.

(0) International Production Number (0) International Publication Number (0) International Publication Number (0) International Publication Number (0) International Publication Number (0) Narch 2021 (0) 503213 A1			Original Article Glutaraldehyde and 2,3-butanediol t
(51) International Pattert Classification: <i>A41R 331007</i> (2005.01) <i>A41P 340</i> (2006.01) <i>A41R 940</i> (2006.01) <i>A41P 340</i> (2006.01)			pericardium for aortic valve biopros
A61P300 (2006.01)	Check for updates	Treatment of wild-type mice with	study
(21) International Application Number: PCT/GB2020052006 (22) International Filing Date:	OPEN ACCESS	2,3-butanediol, a urinary	Kai Ren <sup>14</sup> , Weixun Duan <sup>14</sup> , Zhuowen Liang <sup>24</sup> , Bo Yu <sup>1</sup> , Buvi
(22) International Filing Gate: 01 September 2020 (01.09,2020) (25) Filing Language: English	Mainak Dutta, Birla Institute of Technology and	biomarker of <i>Fmo5<sup>-/-</sup></i> mice,	Shiqiang Yu <sup>1</sup> , Jincheng Liu <sup>1</sup> , Xufeng Wei <sup>1</sup>
(26) Publication Language: English (30) Priority Data:	Science, United Arab Emirates	decreases plasma cholesterol	<sup>1</sup> Department of Cardiovascular Surgery, Xijing Hospital, Air Force Military Me Xijing Hospital, Air Force Military Medical University, Xi'an, China; <sup>1</sup> Jiahe Zhon
1912490.8 30 Auguat 2019 (0.08.2019)     C3     (7) Applicant: UNVERSITY OF GREENWICH (GB/GB);     Old Reval Next College, Public Rev. Greenwich, London	Tapas Mal. The Pennsylvania State University (PSU).	and epididymal fat deposition	Contribution: (I) Conception and design: X Wei, J Liu; (II) Administrative supp Duan, Z Liang; (IV) Collection and assembly of data: B Yu, B Li, C Xue; (V)
S10 9 45 c(4b) (3a Agente BROOKTS PF, Wender House, 6-10 Meant Epinnin Rood, Taubhdga Welds Kent TNI 12E c(2D). 9 3D Designet Static index on drawing indexed by corey	United States Luis Miguel Rodriguez-Alcalà, Universidade Catòlica Portuguesa. Portugal Fabiano Beraldi Calmasini, Sao Francisco University, Brazil	Sunil Veeravalli <sup>1</sup> , Dorsa Varshavi <sup>21</sup> , Flora H. Scott <sup>1</sup> , Dorna Varshavi <sup>21</sup> , Frank S. Pullen <sup>21</sup> , Kirill Veselkov <sup>3</sup> ,	Duan, Z. Lang, (V) Collection and assembly of data: B to, B Li, C. Xue; (V) writing: All authors; (VI) Final approval of manuscript: All authors. *These authors contributed equally to this work. <i>Correspondence to:</i> Shiqiang Yu; Jincheng Liu; Xufeng Wei, Department of Car
Izad of national protection availables, All, AG, AL, AM, AO, AT, AL, AZ, BA, BB, BO, BCB, HIS, NB, RW, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DN, DM, DO, DZ, EY, EH, BG, IS NF, CH, GO, OG, EG, LI (AM, GT, IJN, DZ, EY, EH, BG, IS NF, CH, GO, OG, EG, LI (AM, GT, IJN,	-COBRESPONDENCE Jeromy R. Everett,	Ian R. Phillips <sup>1.4</sup> , Jeremy R. Everett <sup>2</sup> * and Elizabeth A. Shephard <sup>1</sup> *	University, Xi'an, China. Email: yushiq@fmmu.edu.cn; liujch69@sina.com; weisf2
HR, HE, DB, L, NB, RS, HT, JD, JP, KE, KO, KH, LN, NP, MA, WA, ZL, AL, CL, LA, LS, LL, SL, LL, LY, MA, MO, MA, MA, MA, MA, MA, MA, MA, MA, MA, MA,	ji, everettiggreenwich, ac uik Elizabeth A. Shephard, e. shephard@uci.ac.uk 'PRESENT ADDRESS Dorsa Varshavi,	<sup>1</sup> Oppartment of Structural and Molecular Biology, University College London, London, United Kingtom, <sup>1</sup> Nedelay Matabonomics Insearch Group University of Greenolch, Ohatham Martime, Juhied Kingdom, <sup>1</sup> Department of Surgery and Cancer, Faculty of Helschen, Impedia College, London, United Kingdom, <sup>1</sup> School: of Biological and Chemical Sciences, <i>Outern May</i> University of London, University, University	<b>Background:</b> Bovine pericardium can be used for cardiova biocompatibility and durability remain. This study aimed t replacement using an aortic valve prosthesis made of bovine p and 2,3-butanediol (BD).
(84) Designated States innices otherwise indicated, for every kind of regional protection analable: ARIPO (BW, CIL	Doma Varshavi, Faculty of Science, Biological Sciences, University of Alberta, Edmonton, AB,		Methods: The mechanical, plasma protein adsorption, ninhydrin properties of the material (control 1%, GA 1%, GA
GM, KE, LE, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZAWA, Iamidan KM, AZ, HY, KO, KZ, RU, TJ, TML, European (AL, A7, BE, BG, GTL, CY, CZ, DE, DK, PE, PS, TP, RG, GR, REH HPL HE, IS IN TTA TALL LY,	Canada 'Deceased author	We previously showed that Fmo5 <sup>-/-</sup> mice exhibit a lean phenotype and slower metabolic ageing. Their characteristics include lower plasma glucose and	in rats and observed after 8 weeks under microscopy with aliz made from the fully-treated material were implanted in sh
MC, MK, MT, NL, NO, PL, FT, RO, RS, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW,	SPECIALTY SECTION This article was submitted to Upid and	cholesterol, greater glucose tolerance and insulin sensitivity, and a reduction in age-related weight gain and whole-body fat deposition. In this paper, nuclear	control. Effectiveness and safety indicators were observed at 1 Results: Compared with the control group, the GA + BD
Published:	Fatty Acid Research, a section of the journal Frontiers in Physiology	magnetic resonance (NMR) spectroscopy-based metabolite analyses of the urine of Fmo5 <sup>-/-</sup> and wild-type mice identified two isomers of 2,3-butanediol as	and tensile load (both P<0.05), lower plasma protein adsorp digestion, lower ninhydrin value, and higher cross-linking (al
with international search report (Art. 21(3))	Accentro 24 March 2022 Accentro 11 July 2022	discriminating urinary biomarkers of Fmo5 <sup>-/-</sup> mice. Antibiotic-treatment of Fmo5 <sup>-/-</sup> mice increased plasma cholesterol concentration and substantially	GA + BD material showed little or no dissolution; there was by a small amount of fibrosis, with peripheral capillary prolife
IVE	PUBLISHED 08 August 2022 CITATION	reduced urinary excretion of 2,3-butanediol isomers, indicating that the gut microbiome contributed to the lower plasma cholesterol of <i>Fmo5<sup>-1-</sup></i> mice, and	aortic valve leaflets of the experimental animals freely opene abnormal echo was observed. The echocardiographic result
3824	Veeravalli S, Varshavi D, Scott FH, Varshavi D, Pullen FS, Veselkov K, Phillips IR, Everett JR and Shephard EA	that 2,3-butanediol is microbially derived. Short- and long-term treatment of wild-type mice with a 2,3-butanediol isomer mix decreased plasma cholesterol	the two groups. All safety parameters were normal. Conclusions: Modification of bovine pericardium with GA
(4) Title: TREATMENT OF OBESITY AND RELATED CONDITIONS	I2022), Treatment of wild-type mice with 2.3-butanediol, a urinary biomarker of Fmo5 <sup>-/-</sup> mice, decreases plasma	and epididymal fat deposition but had no effect on plasma concentrations of glucose or insulin, or on body weight. In the case of long-term treatment, the	properties for use as an aortic valve prosthesis.
(57) Abstratet: The present invention relates to the use of specific compounds and compositions in the treatment or prevention of obeity; issuini resistance and diabetes and in the reduction of metabolic ageing. Also provided are related non-therapeutic uses for controlling the weight of an individual and for reducting metabolic ageing.	cholesterol and epididymal fat deposition.	effects were maintained after withdrawal of 2,3-butanediol. Short-, but not long-term treatment, also decreased plasma concentrations of triglycerides	Keywords: Aortic valve defect; aortic valve replacement; b glutaraldehvde (GA); butanediol
3	Front. Physiol. 13:859681. doi: 10.3389/tphys.2022.859681	and non-esterified fatty acids. Fecal transplant from Fmo5 <sup>-/-</sup> to wild-type mice	Brown under how (cord) ( Durantering

Preventing obesity, insulin resistance & diabetes **Decreasing cholesterol & fat** 

Reasons for 2,3-BDO in our body!



OH

of bovine heep: a preliminary

ao Jin1, Yimin Zhao3, Chao Xue1,

n, China; <sup>2</sup>Medicine Institute of Orthopedics, Co., Ltd., Hangzhou, China sion of study materials or patients: K Ren, W terpretation: Z Jin, Y Zhao; (VI) Manuscript

Xijing Hospital, Air Force Military Medical

ies, but challenges involving nical testing of aortic valve ed with glutaraldehyde (GA)

collagenase digestion, and All 3 tissues were implanted calcification. Aortic valves l bioprosthesis was used as

gher elongation at breaking idhesion, lower collagenase lantation in rat models, the ition; and it was surrounded ntation in sheep models, the surface was smooth, and no were comparable between

biomaterial with favorable

cation; bovine pericardium;

Improving biocompatibility & durability of transplants

# III. 2,3-BDO manufactured Ses Caltex by GS Caltex is the 1<sup>st</sup> & only bio-2,3-BDO mass producing company

### **2,3-BDO Production Process**



**GS** Caltex

GS Caltex is the first and only company enabling the mass production of high quality 2,3-BDO through microbial fermentation of eco-friendly biomasses.



#### cf. Chemical process for 2,3-BDO production

### **Microbes**



# GS Caltex isolated 2,3-BDO-generating microbes from nature and has developed the most effective 2,3-BDO producer through eco-friendly ways.



#### 2,3-BDO-generating Microbes

GS Caltex has tried to isolate 2,3-BDOproducing microbes **from nature** since 2009.

In 2012, GS Caltex isolated numerous 2,3-BDO producers from on the plain land of Daeduk precinct, South Korea.

Among them, GS Caltex screened microbes that are **greener** than the others.



#### Best 2,3-BDO Producer

GS Caltex has sequenced the genome and characterized their physicochemical properties.

Then, the most effective and **ecofriendly 2,3-BDO producers** were selected for mass production.

These bacteria were registered to Korean Culture Type Collection (KCTC) as properties of GS Caltex.



### **Technologies**





### GS Caltex has developed all core technologies making a breakthrough for the production and recovery of 2,3-BDO through microbial fermentation.



#### 2,3-BDO Fermentation

GS Caltex has developed 2,3-BDO fermentation process using various biomasses, including **non-GMO starch- and sugar-based carbon sources**.

The **fermentation process** developed by GS Caltex enables high-level production of 2,3-BDO with minimum amounts of byproducts at a commercial scale.



#### 2,3-BDO Recovery

GS Caltex has developed core technologies for the **cost-effective** and **eco-friendly** 2,3-BDO recovery from fermentation broth.

The recovery process developed by GS Caltex never uses any toxic chemicals and enables to obtain exceedingly high quality of 2,3-BDO.





GS Caltex GreenDiol process reduces 18-26% of CO<sub>2</sub> emissions compared to fossil-based diols (e.g. DPG, PG) according to the method of ISO 14040/14044



Above results were generated by GS Caltex as of July '23, utilizing Ecoinvent and Sphera DB

\sub GS Caltex

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### **Excellence & Sustainability**



The excellence of technologies, processes, & 2,3-BDO has been officially recognized.

The sustainability of 2,3-BDO has been certified by many global organizations.

GS Caltex successfully registered 2,3-BDO to EU REACH.

- ✓ COSMOS
- ✓ USDA
- ✓ NATRUE
- ✓ VEGAN
- ✓ EU REACH
- ✓ ISO16128: 100% Natural & Natural Origin
- ✓ EWG 1st Green Grade
- ✓ New Excellent Technology Award
- ✓ New Excellent Product Award
- ✓ Jang Young-Sil Award
- ✓ KSBB Award







REACH

COMPLIANCI





# **IV. GS Caltex GreenDiol**

GreenDiol is GS Caltex's trade name for 2,3-BDO





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# As expected, GreenDiol offers multi-layered functions, such as solubilization, unique texture, stabilization, etc., on skin and hair.

Solubilization		
Unique texture	1. Solubilization	<ul> <li>High solubility for active ingredients</li> <li>Better solubilization of ceramides than 1,3-BDO (10x) &amp; DPG (2x)</li> <li>Better dispersion of dyes than 1,3-BG</li> </ul>
	2. Unique texture	<ul><li>Initial body texture</li><li>Quick absorption</li><li>Silky &amp; less sticky</li></ul>
Stabilization	3. Stabilization	<ul><li>Vitamin C stabilization</li><li>Alleviation of vitamin C discoloration</li></ul>
GréenDiol® Anti-inflammation	4. Anti- inflammation	<ul> <li>Reduction of redness</li> <li>Inhibition of pro-inflammatory substances (NF-кВ pathway)</li> </ul>
	5. Penetration	<ul> <li>More effective penetration than 1,3-BDO (4x amount &amp; 2x depth)</li> </ul>
Penetration	6. Preservative boosting	<ul> <li>Superior preservative boosting than 1,3-BDO &amp; 1,3-PDO (~20% more effective)</li> </ul>
Preservative boosting	7. Moisturization	<ul> <li>Superior moisturizing capability than 1,3-BDO (8x)</li> <li>Synergistic moisturizing effects with glycerin</li> </ul>
Moisturization		

## **GreenDiol in Cosmetics & Personal Care Products**



Thanks to 2,3-BDO's unique & distinguished properties, many global cosmetic companies have been adopting GreenDiol for their products.



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#### Solubilization of GreenDiol



1. Solubilization	<ul> <li>High solubility for active ingredients</li> <li>Better solubilization of ceramides than 1,3-BDO (10x) &amp; DPG (2x)</li> <li>Better dispersion of dyes than 1,3-BDO</li> </ul>
2. Unique texture	<ul> <li>Initial body texture</li> <li>Quick absorption</li> <li>Silky &amp; less sticky</li> </ul>
3. Stabilization	<ul><li>Vitamin C stabilization</li><li>Alleviation of vitamin C discoloration</li></ul>
4. Anti-inflammation	<ul> <li>Reduction of redness</li> <li>Inhibition of pro-inflammatory substances (NF-кВ pathway)</li> </ul>
5. Penetration	<ul> <li>More effective penetration than 1,3-BDO (4x amount &amp; 2x depth)</li> </ul>
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#### GS Caltex GreenDiol : Solubilization

## GreenDiol: The Greenest with Multi-functions

#### \*\*\*\*\*\*\*



#### GreenDiol shows a remarkable solubility

- GreenDiol solubilizes ceramides better than 1,3-BDO (10x) & DPG (2x)
- Less ceramides are crystalized (4x) in 2,3-BDO compared to 1,3-BDO



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#### *GreenDiol enables developing high ceramide-containing end-products*



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#### \* \* \* \* \* \* \* \*

#### GreenDiol shows a remarkable solubility

- GreenDiol solubilizes salicylic acid better than other diols (PG, 1,3-BDO, 1,3-PDO)
- Furthermore, GreenDiol disperses colorants more effectively than 1,3-BDO

#### GreenDiol prevents the crystallization of salicylic acid



**19% Salicylic acid in diols** 

21% Salicylic acid in diols

#### 0.01% colorant in 5% diols





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#### The high solubilizing capability of GreenDiol is supported by molecular simulation.

- More 2,3-BDO tends to attach to the head area of ceramides with a vertical angle than 1,3-BDO
- It leads to give more space between ceramide molecules, avoiding stacking & crystalizing



\*\*\*\*\*\*



#### **Unique Texture of GreenDiol**



1. Solubilization	<ul> <li>High solubility for active ingredients</li> <li>Better solubilization of ceramides than 1,3-BDO (10x) &amp; DPG (2x)</li> <li>Better dispersion of dyes than 1,3-BDO</li> </ul>
2. Unique texture	<ul> <li>Initial body texture</li> <li>Quick absorption</li> <li>Silky &amp; less sticky</li> </ul>
3. Stabilization	<ul><li>Vitamin C stabilization</li><li>Alleviation of vitamin C discoloration</li></ul>
4. Anti-inflammation	<ul> <li>Reduction of redness</li> <li>Inhibition of pro-inflammatory substances (NF-кВ pathway)</li> </ul>
5. Penetration	<ul> <li>More effective penetration than 1,3-BDO (4x amount &amp; 2x depth)</li> </ul>
6. Preservative boosting	<ul> <li>Superior preservative boosting than 1,3-BDO &amp; 1,3-PDO (~20% more effective)</li> </ul>
7. Moisturization	<ul> <li>Superior moisturizing capability than 1,3-BDO (8x)</li> <li>Synergistic moisturizing effects with glycerin</li> </ul>



#### GreenDiol has unique texture

- Many chemists are trying to replace conventional polyols with GreenDiol due to its non-sticky finish
- Its non-sticky finish is supported by lower adsorption of pollutants/dusts on skin than other polyols

### Serum with GreenDiol enables non-sticky and fast adsorption & silky-finish touch



Pollutants/dusts adsorption

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#### Stabilization by GreenDiol

	1. Solubilization	<ul> <li>High solubility for active ingredients</li> <li>Better solubilization of ceramides than 1,3-BDO (10x) &amp; DPG (2x)</li> <li>Better dispersion of dyes than 1,3-BDO</li> </ul>
Stabilization	2. Unique texture	<ul> <li>Initial body texture</li> <li>Quick absorption</li> <li>Silky &amp; less sticky</li> </ul>
	3. Stabilization	<ul> <li>Vitamin C stabilization</li> <li>Alleviation of vitamin C discoloration</li> </ul>
GréenDiol <sup>®</sup>	4. Anti-inflammation	<ul> <li>Reduction of redness</li> <li>Inhibition of pro-inflammatory substances (NF-кВ pathway)</li> </ul>
	5. Penetration	<ul> <li>More effective penetration than 1,3-BDO (4x amount &amp; 2x depth)</li> </ul>
	6. Preservative boosting	<ul> <li>Superior preservative boosting than 1,3-BDO &amp; 1,3-PDO (~20% more effective)</li> </ul>
	7. Moisturization	<ul> <li>Superior moisturizing capability than 1,3-BDO (8x)</li> <li>Synergistic moisturizing effects with glycerin</li> </ul>



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#### **GreenDiol stabilizes vitamin C in cosmetic products**

- The distances within the –OH group pairs of 2,3-BDO and vitamin C are much more similar than those of 1,3-BDO and 1,3-PDO.
- It seems for 2,3-BDO to effectively repress discoloration of vitamin C in cosmetic products

#### GreenDiol extends the period of storage for vitamin-containing formulation



\*\*\*\*\*\*



#### Anti-inflammation by GreenDiol

	1. Solubilization	<ul> <li>High solubility for active ingredients</li> <li>Better solubilization of ceramides than 1,3-BDO (10x) &amp; DPG (2x)</li> <li>Better dispersion of dyes than 1,3-BDO</li> </ul>
	2. Unique texture	<ul><li>Initial body texture</li><li>Quick absorption</li><li>Silky &amp; less sticky</li></ul>
Anti-inflammation	3. Stabilization	<ul><li>Vitamin C stabilization</li><li>Alleviation of vitamin C discoloration</li></ul>
GréenDiol <sup>®</sup>	4. Anti-inflammation /soothing	<ul> <li>Reduction of redness</li> <li>Inhibition of pro-inflammatory substances (NF-кВ pathway)</li> </ul>
	5. Penetration	<ul> <li>More effective penetration than 1,3-BDO (4x amount &amp; 2x depth)</li> </ul>
	6. Preservative boosting	<ul> <li>Superior preservative boosting than 1,3-BDO &amp; 1,3-PDO (~20% more effective)</li> </ul>
	7. Moisturization	<ul> <li>Superior moisturizing capability than</li> <li>1,3-BDO (8x)</li> <li>Synergistic moisturizing effects with glycerin</li> </ul>



#### GreenDiol represses inflammation on skin (soothing)

- 2,3-BDO has significantly superior anti-inflammatory effects than 1,3-BDO and 1,3-PDO
- GreenDiol can give higher anti-inflammatory effect with similar cost of active ingredient (D-panthenol)

### GreenDiol replaces conventional anti-inflammation agents



#### SKI: with active ingredients



D-panthenol GreenDiol Negative

INCI name	Formula (%)		
	Negative	D-Panthenol	GreenDiol
Water	95.21	94.21	89.66
Disodium EDTA	0.02	0.02	0.02
Carbomer	0.14	0.14	0.14
Glycerin	3.00	3.00	3.00
Hydroxyethylcellulose	0.02	0.02	0.02
Dexpanthenol	-	1.00	-
GreenDiol	-	-	5.55
Tromethamine	0.11	0.11	0.11
1,2-Hexanediol	1.50	1.50	1.50





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#### **GreenDiol represses inflammation on skin**

- 5 factors participating in inflammation on skin have been observed with GreenDiol and dexamethasone
- GreenDiol has also served anti-inflammatory effects like dexamethasone

#### GreenDiol shows a similar anti-inflammatory effect to steroids



Manuscript in preparation

Effectiveness of GreenDiol on anti-inflammation





*Ex vivo* histological & immunological verification







\*Pre-treated with 50 ppm PMA (phorbol 12-myristate 13-acetate)

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#### **Penetration of GreenDiol**



1. Solubilization	<ul> <li>High solubility for active ingredients</li> <li>Better solubilization of ceramides than 1,3-BDO (10x) &amp; DPG (2x)</li> <li>Better dispersion of dyes than 1,3-BDO</li> </ul>	
2. Unique texture	<ul><li>Initial body texture</li><li>Quick absorption</li><li>Silky &amp; less sticky</li></ul>	
3. Stabilization	<ul><li>Vitamin C stabilization</li><li>Alleviation of vitamin C discoloration</li></ul>	
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7. Moisturization	<ul> <li>Superior moisturizing capability than 1,3-BDO (8x)</li> <li>Synergistic moisturizing effects with glycerin</li> </ul>	



#### GreenDiol more effectively penetrates dyes into skin and hairs than other diols

- The amounts of a dye in skin tissues that were treated with or immersed in GreenDiol have shown 4x or 10x higher than those of 1,3-BDO, respectively.
- A commercial color shampoo containing GreenDiol have shown remarkable hair-dying performance

### GreenDiol can quickly dye the hair and retain the color longer for color shampoo





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#### **Preservative Boosting by GreenDiol**



7. Moisturization	<ul> <li>Superior moisturizing capability than 1,3-BDO (8x)</li> <li>Synergistic moisturizing effects with glycerin</li> </ul>
6. Preservative boosting	<ul> <li>Superior preservative boosting than 1,3-BDO &amp; 1,3-PDO (~20% more effective)</li> </ul>
5. Penetration	<ul> <li>More effective penetration than 1,3-BDO (4x amount &amp; 2x depth)</li> </ul>
4. Anti-inflammation	<ul> <li>Reduction of redness</li> <li>Inhibition of pro-inflammatory substances (NF-кВ pathway)</li> </ul>
3. Stabilization	<ul> <li>Vitamin C stabilization</li> <li>Alleviation of vitamin C discoloration</li> </ul>
2. Unique texture	<ul> <li>Initial body texture</li> <li>Quick absorption</li> <li>Silky &amp; less sticky</li> </ul>
1. Solubilization	<ul> <li>High solubility for active ingredients</li> <li>Better solubilization of ceramides than 1,3-BDO (10x) &amp; DPG (2x)</li> <li>Better dispersion of dyes than 1,3-BDO</li> </ul>

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#### GreenDiol has a better preservative boosting effect compared with other polyols

- MIC test results show better preservative effect of GreenDiol than other diols
- In particular, GreenDiol boosts the effects of conventional preservatives (e.g. phenoxyethanol)

#### GreenDiol decreases the use of preservatives reducing irritation



\* For bacteria: Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus For fungi: Aspergillus niger, Candida albicans



\* Standard bacteria: E. coli, P. aeruginosa, S. aureus \*\*Standard fungi: Aspergillus brasiliensis, Aureobasidium pullulans, C. albicans, Penicilliumm citrinum

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#### **Moisturization by GreenDiol**



7. Moisturization	<ul> <li>Superior moisturizing capability than 1,3-BDO (8x)</li> <li>Synergistic moisturizing effects with glycerin</li> </ul>
6. Preservative boosting	<ul> <li>Superior preservative boosting than 1,3-BDO &amp; 1,3-PDO (~20% more effective)</li> </ul>
5. Penetration	- More effective penetration than 1,3-BDO (4x amount & 2x depth)
4. Anti-inflammation	<ul> <li>Reduction of redness</li> <li>Inhibition of pro-inflammatory substances (NF-κB pathway)</li> </ul>
3. Stabilization	<ul> <li>Vitamin C stabilization</li> <li>Alleviation of vitamin C discoloration</li> </ul>
2. Unique texture	<ul> <li>Initial body texture</li> <li>Quick absorption</li> <li>Silky &amp; less sticky</li> </ul>
1. Solubilization	<ul> <li>High solubility for active ingredients</li> <li>Better solubilization of ceramides than 1,3-BDO (10x) &amp; DPG (2x)</li> <li>Better dispersion of dyes than 1,3-BDO</li> </ul>

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#### GreenDiol has higher water retention capability

- Higher polarities at the –OH groups of 2,3-BDO leads to higher water retention than other diols
- Unexpectedly, GreenDiol shows moisturization boosting effect with glycerin



#### GreenDiol strengthens and lingers the moisturizing effect





#### If you would like to discuss this report, please contact

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