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The Importance of Cooperating with China in the Global Health System

A Importância da Cooperação com a China no Sistema Global de Saúde

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ABSTRACT

The Guangdong-Hong Kong-Macao Greater Bay Area (GBA), which was established in 2017, consists of Hong Kong, Macao and nine cities in the Guangdong province of China. Since then, the Chinese central government and the local governments have established new policies to favour the healthcare development in the GBA. This article aims to summarise the recent education and business opportunities related to healthcare development in the GBA, and the economic benefits of the GBA, especially in Traditional Chinese Medicines and medical devices industries. Lastly, the advantages of Macao as a pharmaceutical technology transformation platform to the Portuguese-Speaking Countries is also discussed.

KEYWORDS

Guangdong-Hong Kong-Macao Greater Bay Area, GBA, proprietary Chinese medicine, Traditional Chinese Medicine (TCM), medical education, pharmaceutical industry, medical device, healthcare.

RESUMO

A Grande Área da Baía de Guangdong-Hong Kong-Macau (GAB), criada em 2017, é composta por Hong Kong, Macau e nove cidades da província chinesa de Guangdong. Desde então, o governo central chinês e os governos locais estabeleceram novas políticas para favorecer o desenvolvimento da saúde na GAB. Este artigo tem como objetivo resumir as recentes oportunidades de educação e de negócios relacionadas com o desenvolvimento da saúde na GAB, bem como os benefícios económicos da GAB, especialmente nas indústrias de Medicina Tradicional Chinesa e dos dispositivos médicos. Por último, são discutidas as vantagens de Macau como plataforma de transformação da tecnologia farmacêutica para os Países de Língua Portuguesa.

PALAVRAS-CHAVE

Grande Área da Baía de Guangdong-Hong Kong-Macau (GAB), medicina chinesa proprietária, Medicina Tradicional Chinesa (MTC), educação médica, indústria farmacêutica, aparelhos médicos, assistência médica.

An introduction to the GBA and the opportunities emerged in pharmaceutical and medical landscape

The Guangdong-Hong Kong-Macao Greater Bay Area (also referred as the GBA in this article) is a city-cluster consisting of two Special Administrative Regions (SARs, Hong Kong and Macao) plus nine neighbouring cities (Guangzhou, Shenzhen, Dongguan, Foshan, Zhongshan, Huizhou, Jiangmen, Zhuhai, Zhaoqing) in Guangdong Province, China. The GBA has a total area of 56,000 km^2 (almost half the size of Portugal, 92,212 km^2). In 2020, a population of approximately 70 million people was recorded (5% of China's total population). This city cluster of the GBA has the highest GDP per capita among all cities in China, and the strongest economic performance growth in southern China (12% of national GDP).

High-quality medical services are important for the healthcare of local citizens, and for further development of the health and medical industries in the GBA. The Healthcare Access and Quality (HAQ) index published in the Lancet indicates a lower overall HAQ index of China compared with those of the other well-developed countries (Fullman et al., 2018). However, the HAQ index of Guangdong, China is comparable to those of metropolitan regions worldwide. The population of the GBA rose from 61.15 million in 2009 to 72.65 million in 2019, corresponding to 5% of China's total population (Statista, 2021), a growing demand for reliable and affordable medical services is anticipated in the region. There are currently over 25000 medical service providers in the GBA (Department of Health, 2021; Health Commission of Guandong Province, 2020; Simões et al., 2017; Statistics and Census Service, 2020), and 28 universities that offer medicine, Chinese medicine and pharmacy programmes, providing young, high-calibre talents in the related sectors in the GBA.

There are series of policies and campaigns introduced under the GBA initiative, providing opportunities for the higher education and the related industry. Sharing of teaching and research resources within the region is promoted, accelerating the medical development. The policy also provides opportunities for the local medical and pharmaceutical products, more importantly, the GBA allows the industry not only flourish within the region, but also radiate to the global market through the special roles of Hong Kong and Macao.

Pharmaceutical and Medical Device Industries: Dual Engines of Economic Growth in the GBA

The pharmaceutical and medical device industries in the GBA are two of the fastest expanding sectors and are driving economic growth in the region. The numbers of companies (based in the GBA) related to biopharmaceutical and biomedical industries listed on Hong Kong, Shenzhen and Shanghai stock markets are summarized in Table 1 (广东省药品监督管理局, 2020; 平安证券研究所, 2019). For instance, the total industrial output value of the pharmaceutical industry in Chinese medicine is 45.71 billion RMB. Among them, the sales of proprietary Chinese medicine are 33.43 billion RMB in the GBA, contributing more than 11% of the total sales in the country and ranking as the top-selling proprietary Chinese medicine in China. In fact, there are 170 proprietary Chinese medicine manufacturers or enterprises in the GBA, among which nine have an annual output value of over 1 billion RMB. For example, Guangzhou Pharmaceutical Holdings Limited (GPHL) is the largest manufacturer of proprietary Chinese medicine in China. The total number of medical device production enterprises in the GBA is around 60,000 (Table 2). In general, medical device production enterprises outnumber pharmaceutical enterprises, but usually exhibit greater variation in terms of company size and the scale of production.

Table 1 – Summary of the biopharmaceutical and biomedical companies in the GBA, listed on the China A-shares and Hong Kong stock exchanges

	China A shares	New OTC market	HK stocks
Medical devices	13	29	1
Chemical medicine	8	10	9
Biological products	5	17	1
Health service	4	11	3
Pharmaceutical Commerce	4	4	0
Traditional Chinese Medicine	4	2	2
Total	38	73	16

Table 2 – Number of medical device production enterprises in the GBA.

City/ SAR	Class I medical device production enterprise	Class II and III medical device production enterprise
Guangzhou	667	16166
Shenzhen	449	15547
Zhuhai	77	2420

City/ SAR	Class I medical device production enterprise	Class II and III medical device production enterprise
Foshan	232	4688
Jiangmen	32	2684
Zhaoqing	10	1208
Huizhou	28	3022
Zhongshan	57	4811
Dongguan	105	7513

Class I medical devices are devices which safety and effectiveness can be ensured through routine administration. Class II medical devices are devices which require control to ensure safety and effectiveness. Class III medical devices are devices that are designated for implantation into human body, or for life support or sustenance; these may pose a potential risk to the human body, so safety and effectiveness must be strictly controlled

Harmonization of Regulations for the Registration of Pharmaceutical Products and Medical Devices in the Greater Bay Area, China: Opportunity for Hong Kong and Macao as "Golden Gateways" to the Chinese Market

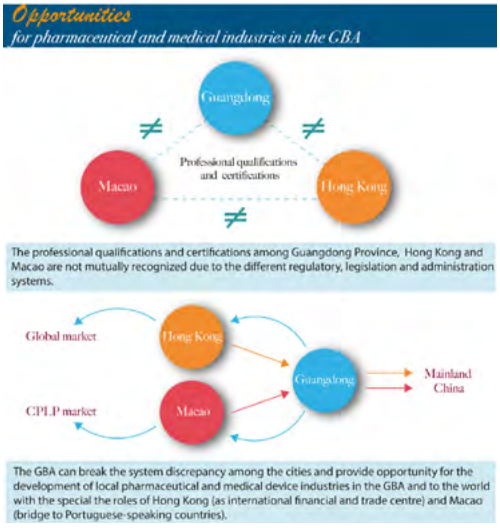

Figure 1 – Opportunities for pharmaceutical and medical industries in the GBA

The development of pharmaceutical and medical device industries in the GBA plays a crucial role in the economic development of the region. Before the handover of both SARs to China, Hong Kong followed the British legislative system, while Macao followed that of Portugal. One of the major challenges to establish

the GBA is to resolve the barriers caused by the different regulatory, legislation and administration systems among Guangdong Province, Hong Kong and Macao. Developing new policies and regulations to reduce the discrepancies among these cities is indispensable to promote business and trading throughout the GBA and, more importantly, to fully utilize Hong Kong and Macao as golden gateways to facilitate business and trading with other countries.

In 2019, after the establishment of the GBA, several agreements and cooperative frameworks have been jointly issued by Guangdong, Hong Kong and Macao to speed up the development of the GBA. In the same year, Guangdong, Hong Kong and Macao jointly issued the Greater Bay Area Health Co-operation Consensus. This consensus prioritised six aspects for future development, summarised in Table 3. The Food and Health Bureau of Hong Kong and National Medical Products Administration also signed the Co-operation Agreement on Regulation of Drugs. This agreement focuses on the establishment of new regulations for drugs, medical devices and Chinese medicines with the aim of attracting local and multinational pharmaceutical, biomedical and health technology companies to register new pharmaceutical products and medical devices in Hong Kong, and expand their business to the GBA thereby benefiting patients in need. A Memorandum of Guangdong-Hong Kong-Macao Greater Bay Area Chinese Medicine Cooperation was also signed, to promote coordinated nurturing of talented Chinese medicine practitioners in Guangdong, Hong Kong and Macao. Moreover, the Work Plan for Regulatory Innovation and Development of Pharmaceutical and Medical Devices in the Guangdong-Hong Kong-Macao Greater Bay Area was announced at the end 2020, which covers six areas of development including authorization for the sale and marketing of Hong Kong- and Macao-registered drugs, and medical devices, in the GBA. This Work Plan has six key tasks (listed in Table 4), the first of which is changing the authority for approval of the use of medical devices in Guangdong Province of the GBA from the State Council to the People's Government of Guangdong Province. More recently, in April 2021, the Guangdong Provincial Medical Products Administration announced "The Measure", i.e., authorizing designated healthcare institutions in Guangdong Province of the GBA to use Hong Kong--registered drugs and medical devices to meet urgent clinical needs, subject to the approval of Guangdong Province. In summary, since the establishment of the GBA, the government of Guangdong and both SARs have been making efforts to resolve the regulatory discrepancy that hinder free trade of medical and pharmaceutical products in GBA (Table 5). Furthermore, in March 2021, the Chinese

government announced the country's 14th Five-Year Plan for economic and social development (14th Five-Year Plan) (Government Information Bureau [GCS], 2021). Through this plan, Macao has an opportunity to strengthen cooperation with other cities in the GBA, especially with its neighbouring city – Hengqin in Zhuhai. Both cities will work closely in different areas, such as the development of cutting-edge industry, especially for the manufacture of traditional Chinese medicine (TCMs). Moreover, both cities will establish a diversified economic and financial environment to achieve green objectives and shared development in the GBA, the Macao government also advocates the development of Green Finance to contribute to diversified financial development in the GBA (GCS, 2020). All of these policies aim to contribute to the development of a modern economic system and comprehensive opening up of the country.

In conclusion, all of the recent agreements and policies focusing on pharmaceutical and medical development in the GBA, by making good use of Hong Kong (as international financial and trade centre) and Macao (as a bridge to Portuguese-speaking countries). These policies also safeguard healthcare quality for the citizens, and encourage medical and economic development in the GBA via co-operative frameworks among the cities of the GBA.

Table 3 – The six aspects covered in the Greater Bay Area Health Co-operation Consensus jointly issued by Guangdong, Hong Kong and Macao (GCS, 2019; Hong Kong Trade Development Council [HKTDC], 2019)

	Chinese	English	Portuguese
	2019《粵港澳大灣區衛生健康合作共識》	Guangdong--Hong Kong-Macao Health Cooperation Consensus	"Protocolo de Saúde da Grande Baía Guangdong-Hong Kong-Macau"
1	推動優質醫療資源緊密合作	Closer co-operation with regard to the use of premium medical resources	promoção da cooperação estreita em recursos médicos de qualidade
2	加強公共衛生應急領域合作	Strengthening co-operation to tackle public health emergencies	fortalecimento da cooperação em áreas de emergência de saúde pública
3	深化中醫藥領域創新合作	Greater co-operation in the development and exploitation of traditional Chinese medicine	aprofundamento da cooperação em inovação na área da medicina tradicional chinesa,

	Chinese	English	Portuguese
4	拓展科研和服務領域合作	Expanding co-operation in the areas of scientific research and related services	exploração da cooperação nas áreas de investigação e serviços
5	強化人才培養和診療合作	Strengthening personnel training in co-operation	e intensificação do treinamento de recursos humanos e da formação de diagnóstico e tratamento
6	以人民健康為中心	Encouraging increasingly patient-centric medical services	Centrado pela saúde da população

Table 4 – Six key tasks listed in the Work Plan for Regulatory Innovation and Development of Pharmaceutical and Medical Devices in the Guangdong-Hong Kong-Macao Greater Bay Area, announced at the end 2020 (Constitutional and Mainland Affairs Bureau, 2020)

1	Changing the approval authority from the State Council to the People's Government of Guangdong Province, for the use of drugs that are marketed in Hong Kong and Macao and urgently needed for clinical use in designated medical institutions operating in nine cities in the GBA;
2	Suspending the implementation of Article 11 of Paragraph 2 of the regulations on the supervision and administration of medical devices in nine cities in the GBA, and requesting that designated medical institutions operating in the region that shall use medical devices in urgent clinical need, and have been purchased and used by public hospitals in Hong Kong and Macao and have advanced clinical applications, to obtain approval from Guangdong Provincial Government;
3	Accelerating the review process by the National Medical Products Administration for construction of the GBA sub-centre for drug and medical device evaluation and inspection;
4	Encouraging the development of traditional Chinese medicine in the Traditional Chinese Medicine Science and Technology Industrial Park, and co-operation between Guangdong and Macao in Hengqin;
5	Reforming the system of drug marketing by license holders and medical device registrants in the GBA; and
6	Establishing a drug import port in Zhongshan. The five safeguard measures include establishing a coordination mechanism, improving supporting systems, implementing supervision responsibilities, strengthening subject accountability and improving remedy systems.

Table 5 – Timeline for the announcement of relevant policies promoting the development of the GBA (Health Bureau, 2019; Hong Kong SAR Government, 2019a, 2019b, 2021; HKTDC, 2020; Macao SAR Government, 2021)

Announcement period	Event	Government involved
2019-02	Guangdong-Hong Kong-Macao Health Cooperation Consensus	Guangdong, Hong Kong, Macao
2019-05	Co-operation Agreement on Regulation of Drugs and Co-operation Agreement on Construction, Research and Management of Chinese Medicines Herbarium	Guangdong, Hong Kong
2019-12	Memorandum of Cooperation on Advancement, Innovation and Development of Traditional Chinese Medicine in the Great Bay Area of Guangdong-Hong Kong-Macao)	Guangdong, Hong Kong, Macao
2020-04	Legal framework for registration and management of traditional Chinese medicines	Macao
2020-12	Work Plan for Regulatory Innovation and Development of Pharmaceutical and Medical Devices in the Guangdong-Hong Kong-Macao Greater Bay Area (the work plan)	Guangdong, Hong Kong, Macao
2021-04	Allowing designated healthcare institutions operating in the Guangdong-Hong Kong-Macao Greater Bay Area (GBA) to urgently use Hong Kong-registered drugs and medical devices used in Hong Kong public hospitals for clinical applications (the measure).	Guangdong, Hong Kong, Macao
2021-05	Master Plan of the Development of the Guangdong-Macao Intensive Cooperation Zone in Hengqin	Guangdong, Macao

Two Decades of Revolutionary Changes in Traditional Chinese Medicine Education, Research and Industry in Macao (2002-2021): An Opportunity for Cooperation between the GBA and Portuguese-Speaking Countries

In February 2002, the University of Macau (UM) established the Institute of Chinese Medical Sciences (ICMS). At that time, the ICMS offered two MSc programmes in Chinese Medicinal Science and Medicinal Administration, and an additional 2-year PhD programme in Biomedical Sciences. Within 9 years, the ICMS has established postgraduate study programmes, high-quality academic research and extensive international collaborations. In December 2010, with approval and support from the Ministry of Science and Technology, the UM-ICMS also established the State Key Laboratory of Quality Research in Chinese Medicine (SKL-QRCM) – the first ever SKL in the broad field of Chinese medicine. In September 2021, the UM established a new undergraduate programme in Pharmaceutical Sciences and Technology, further nurturing talents in the field of pharmaceutical science and

pharmaceutical management. The SKL-QRCM has subsequently been developing rapidly, a rapidly growing presence both at home and abroad. The SKL has devoted itself to promoting research on Chinese medicine and nurturing talent in the multidisciplinary fields of biomedical and pharmaceutical sciences.

On 6th March 2011, a Framework Agreement on Cooperation between Guangdong and Macao was signed by the governments of both regions. A Traditional Chinese Medicine Science and Technology Industrial Park of collaboration between Guangdong and Macao (hereinafter referred to as "GMTCM Park") was officially inaugurated in Hengqin, Zhuhai City, in April 2011. It is developed, operated and managed as a joint venture between Macao and Hengqin under this agreement. GMTCM Park covers an area of 500,000 square meters with a total development area of nearly 1.4 million square meters. GMTCM Park has developed specialized public service platforms that adhere to the standards of mainland China and the European Union, including Good Manufacturing Practice (GMP) pilot-scale production, research, development and testing, as well as incubation areas to nurture different types of businesses. As of early September 2020, 200 companies have registered at GMTCM Park, covering areas such as TCM, healthcare products, medical apparatus, medical services and biomedicine. Other than the development of cutting-edge high technology industries, especially for the manufacture of TCM, the collaboration between Macao and Hengqin has also been planning to establish a new stock exchange centre, in addition to the three existing stock exchange centres in Hong Kong, Shenzhen and Shanghai in China. The Macao government advocates the centre to focus on the development of Green Finance to promote diversified financial development in the GBA (Government Information Bureau, 2020). Some investment experts expect the emerging TCM industry will be benefited from an investment fund after setting up the Macao stock exchange centre. In 2020, the Macao government announced the draft of the legislation for the registration and management of TCM in Macao. It is granted regulatory approval in July 2021 and will be effective from January 2022 ("Registration of Proprietary Chinese Medicines", 2021). Completion of the legislation for registration and management of TCM will open an opportunity for the development of TCM products in Macao, possibly expanding into the GBA market in future. In October 2021, the Executive Council (2021a, 2021b) completed the discussion on establishing the Drug Administration Bureau and restructure of the Health Bureau, setting up the Department of Traditional Chinese Medical Service Development, which is effective on 1 January 2022.

Why Traditional Chinese Medicine (TCM)? Examples of New Natural Medicinal Products Addressing Unmet Medical Needs

Cardiovascular disease, cancer, obesity and neurodegenerative disorders are closely interrelated and increasingly severe public health issues due to demographic changes and overall improved medical care, resulting in a larger aged population. Global disease projections indicate that the healthcare burden of these diseases will continue to rise. TCM has been used to prevent and treat multi-faceted diseases in China and other Asian countries. Medicinal plants and natural materials are potential rich sources of novel pharmaceutical products. TCM has been used clinically for a long time in China, and also plays an important role in the current medical system of the country. Some pharmaceutical companies have increased their investment in the development of natural medicinal products targeting international markets. Two examples of pharmaceutical products are briefly introduced below.

China Approved Seaweed-based Oligomannate, the World's First New Alzheimer's Drug in 20 Years

Neurodegenerative diseases are the most prevalent senile diseases in aging populations (especially those aged over 70 years), including Parkinson's disease (PD) and Alzheimer's disease (AD). Cognitive decline, slow and involuntary movements, progressive dementia, and changes of personality are the most common symptoms of these two diseases; however, the psychological disorders associated with PD and AD should not be overlooked. Anxiety and depression are secondary changes seen not only in neurodegenerative diseases, but also in other brain disorders. This overlap indicates that brain disorders are complex. Since AD and PD are multifactorial disorders without effective cures, nearly all of the drugs on the market focus to alleviate the symptoms. Natural products contain multiple chemical constituents, which are more effective than single chemicals in addressing the pathogenesis of multifactorial disorders through their effects on multiple targets. This explains why drugs developed from natural products with preventive activities against brain disorders are particularly desirable. For example, epidemiological data suggests that elderly people who regularly consume seaweed are less susceptible to AD; therefore, sodium oligomannate (GV-971®), a marine algae-derived oral oligosaccharide, has been developed and was conditionally approved in China for the treatment of mild-to-moderate AD (to improve cogni-

tive function) in November 2019 (Syed, 2020). Unlike most small molecule drugs on the market, which act on specific neuronal cells, GV-971® is a mixture of oligosaccharides regarded as a macromolecule, and therapeutically remodels gut microbiota and suppresses gut bacterial amino acids-shaped neuroinflammation to inhibit AD progression (Figure 2) (X. Wang et al., 2019).

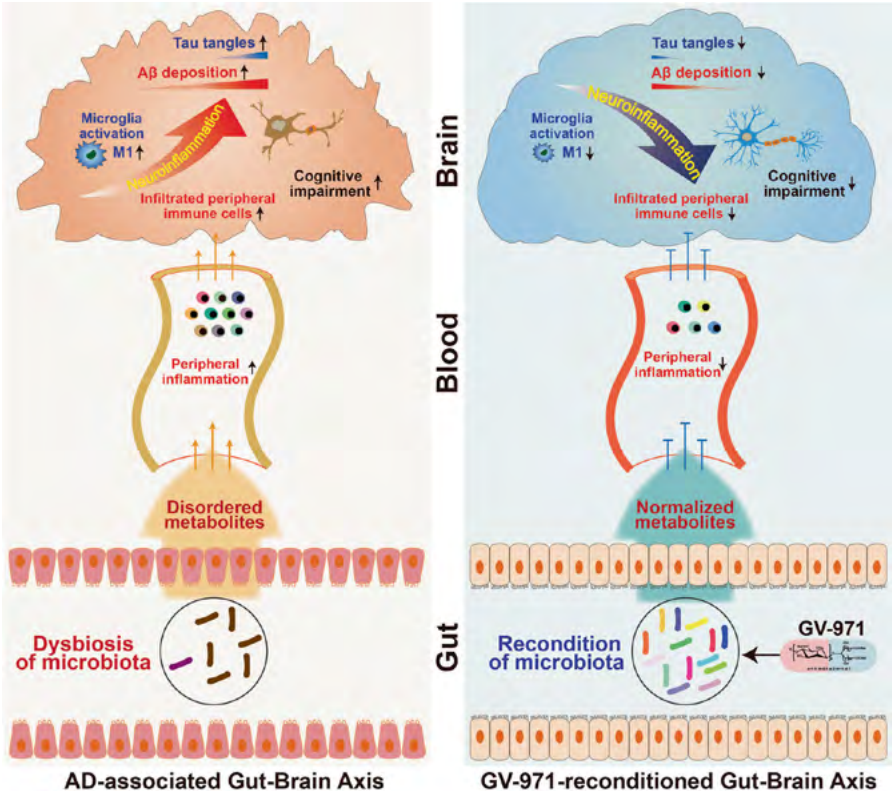

Figure 2 – Schematic diagram of the gut-brain axis involved in AD progression and the intervention strategy. Figure adapted from Figure 6 in "Sodium oligomannate therapeutically remodels gut microbiota and suppresses gut bacterial amino acids-shaped neuroinflammation to inhibit Alzheimer's disease progression" by Wang, X., Sun, G., Feng, T. *et al.*, used under CC BY 4.0

A phase II randomized trial of sodium oligomannate in Alzheimer's dementia took place between 24 October 2011 and 10 July 2013 (T. Wang et al., 2020). The 24-week multicenter, randomized, double-blind, placebo parallel controlled clinical trial was conducted in China. In total, 242 AD patients were randomly divided into three groups receiving GV-971 900 mg, 600 mg, or a placebo capsule during the treatment period. From the results, after treatment with 900 mg GV-971, the ADAS-cog12 and CIBIC-Plus scores were higher than in the other

two groups. Therefore, this phase II trial provided evidence that GV-971 was safe and well tolerated. GV-971 900 mg was chosen for a now-complete phase III clinical, double-blind, placebo-controlled trial involving Chinese patients with mild--to-moderate AD patients (Xiao et al., 2021). A total of 818 participants from 34 regions in China were randomized to placebo or GV-971 (900 mg) for 36 weeks. A significant drug-placebo difference on the ADAS-Cog12 favoring GV-971 was present at each measurement time point, from the week 4 visit onward. Moreover, GV-971 demonstrated significant efficacy for improving cognition, with sustained improvement seen across all observation points in the 36-week trial. Therefore, this phase III trial provided evidence that GV-971 is safe and well-tolerated. Subsequently, Green Valley, the sponsor of GV-971, planned to conduct a phase III trial (Green Memory) in the USA, Europe and Asia in early 2020, to facilitate global regulatory approval of sodium oligomannate (Reuters, 2019).

FuZheng HuaYu Formula (FZHY) is Being Developed as the First Anti-liver Fibrotic Drug in the US

Nonalcoholic fatty liver disease (NAFLD) can be divided into two major subtypes: simple steatosis and nonalcoholic steatohepatitis (NASH). NAFLD is the most common chronic liver disease in most countries and regions, including the United States, Asia, the Middle East, and Europe (Loomba & Sanyal, 2013). The worldwide prevalence of NAFLD has been estimated at 25.24% and shows an increasing trend in accordance with the high prevalence of obesity, diabetes, hyperlipidemia and metabolic syndrome (Fazel et al., 2016; López-Velázquez et al., 2014; Younossi et al., 2016). Most patients do not progress to cirrhosis, which is mainly characterized by steatosis (especially macrovascular steatosis), while almost 20% of patients will develop NASH, a progressive liver disease (Angulo, 2002). Patients with NASH usually develop liver steatosis, more severe lobular and portal inflammation, and ballooning, and have a higher chance of progressing to fibrosis, cirrhosis and hepatocellular carcinoma (Brunt, 2001). Clinically, NAFLD is often accompanied by elevated serum aminotransferases, accumulation of fat with more than 5% hepatocytes, with no history of alcohol abuse (Loomba & Sanyal, 2013; Méndez--Sánchez et al., 2007). There is no drug approved for effective management of NAFLD, and TCM has been used for managing different liver diseases in China for many years. The pathogenesis of NAFLD includes spleen vacuity, liver stagnation, and phlegm-damp obstruction according to the theory of TCM.

FuZheng HuaYu formula (FZHY), which is composed of six herbs, is a proprietary Chinese medicine preparation (No: Z20050546) approved by China State Food and Drug Administration (SFDA) for treatment of liver fibrosis (J. Chen et al., 2019). It has been reported that FZHY has efficacy for liver fibrosis, post-hepatic cirrhosis, and the prevention of hepatic encephalopathy and esophageal and gastric variceal bleeding (Dong et al., 2018; Wu et al., 2020). Moreover, an anti-fibrotic effect of FZHY was confirmed in patients with chronic hepatitis C, in a United States Food and Drug Administration (US FDA)-approved phase II clinical trial completed in 2013 (Y. Chen et al., 2020). The underlying mechanisms of FZHY's effects are primarily related to the suppression of pathways involved in autocrine activation on both hepatic stellate cells (HSCs) and fibrotic liver tissue, and the regulation of the expression of related cytokines, such as vascular endothelial growth factor (VEGF) (Liu et al., 2002), transforming growth factor-β1 (TGF-β1) (Q. L. Wang et al., 2012), α-smooth muscle actin (α-SMA) (Yang, 2013), p38 mitogen-activated protein kinase (MAPK), stress-activated protein kinase, and Jun N-terminal kinase (SAPK/JNK) (Q. Wang et al., 2013). While the US FDA has not yet approved any anti-liver fibrotic drugs, further phase III clinical trials of FZHY formula with satisfactory results will warrant its marketing as a botanical drug in the US.

A Showcase for Successful Technology Transfer and Cooperation between a University in Macao and a Portugal Biopharmaceutical Company

In 2014, in the presence of Portuguese President Aníbal António Cavaco Silva, UM signed a statement of work with a Portugal biopharmaceutical company, TechnoPhage, to strengthen the collaboration between Macao and Portugal in the development of innovative pharmaceutical products and commercialization of Chinese medicines (Figure 3). The agreement between UM and TechnoPhage signaled the official start of the collaboration, including technology transfer of the PD-001 project. A research team led by Prof Simon Ming-Yuen Lee, from UM, discovered bioactive PD-001 molecules, as antidotes for PD and AD, in Macao; the research was initially funded by the Science and Technology Development Fund of Macao, and recently filed a number of patents in Europe, the United States, China and Japan. As a biotechnology company based in Portugal, TechnoPhage will register and manufacture PD-001 into novel food ingredients for use in Europe (as the primary target), and eventually will expand the marketing of PD-001 as a

dietary supplement in the global markets. This project will be the first to develop pure compounds from TCM as a novel food ingredient in Europe. The collaboration reflects Macao's role as a service platform for health and pharmaceutical products produced jointly by China and Portuguese-speaking countries.

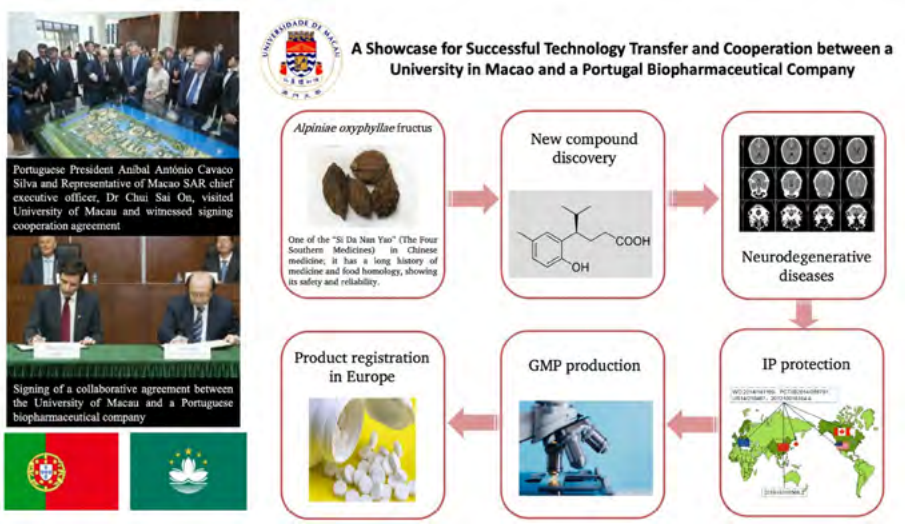

Figure 3 – Technology transfer and cooperation between a University in Macao and a Portugal biopharmaceutical company

Recent Activities/Schemes Promoting Macao to Develop into the Bridge Linking the GBA and the Portuguese-speaking World

To coordinate the "innovation-driven development strategy" mentioned in the "Outline Development Plant for the Guangdong-Hong Kong-Macao Greater Bay Area" and take the advantage of Macao's special role as a service platform for health and pharmaceutical products between China and Portuguese-speaking countries, there are various platforms and schemes strengthen the pharmaceutical connection in recent years.

The government provides resources for scientists and young entrepreneurs with different campaigns. The Science and Technology Development Fund (FDCT), instituted by the Macao government, has the mission to improves research capabilities, innovation as well as competitiveness in Macao. The FDCT offers "FDCT-EC Project" to support Macao research teams participating in the Horizon Europe

program, which is the EU's key funding programme for research and innovation (Science and Technology Development Fund [FDCT], n.d.).

The government established a company "Parafuturo de Macau Investment and Development Limited" with the mission to implement government guidance to proactively embrace new opportunities in the GBA, for instance, managing the "Guangdong-Macao in-depth cooperation zone" under the GBA development strategy. Economic and Technological Development Bureau organized different competitions and were implemented by the company. The "Youth Innovation and Entrepreneur Exchange Programme for China and Portuguese-speaking Countries" was first held in 2017, with the aim to reinforce Macao's role as a commercial and trade cooperative service platform connecting China and Portuguese-speaking countries. The programme provides Macao young entrepreneurs opportunities to learn the local market environment and discover chances for cooperation and development (Macao Young Entrepreneur Incubation Centre [MYEIC], n.d.-a). In 2021, "Innovation and Entrepreneurship Competition (Macao) for Technology Enterprises from Brazil and Portugal" was launched, inviting innovative projects from Brazil and Portugal to soft-launch the business in the Great Bay Area (MYEIC, n.d.-b).

There are also non-profit organizations with members composed of scientists, scholars and experts from the industry to promote and drive the exchange and cooperation between China and Portuguese speaking countries. For examples, Macau Pharmacology Association (MPA)[1], Consortium of 'Belt and Road' and Portuguese-Speaking Countries for Natural Medicine Innovation (Macao) (BPNMI)[2]; China-Portuguese-Speaking Countries Association of Natural Products and Bioeconomy (Macao)[3]; and Macao Association for Scientific Cooperation between China and Portuguese Speaking Countries[4]. The MPA organised the First Sino--Community of Portuguese Language Countries (CPLP) Symposium on Natural Products and Biodiversity Resources at University of Macau in 2018 (Macao Trade and Investment Promotion Institute [IPIM], 2021), the conference abstracts were collected and published in *Chinese Medicine* (2018). In 2021, the MPA and BPNMI co-organised the Third Sino-CPLP Symposium on Natural Products and Biodiver-

[1] Contact information: https://linkedin.com/company/bpnmi-consortium

[2] Contact information: https://linkedin.com/company/macau-pharmacology-association

[3] Contact information: https://linkedin.com/company/china-portuguese-speaking-countries-association-of-natural-products-and-bioeconomy-macao

[4] Website: www.ascmac.org

sity Resources, this international symposium created a platform for scholars from different countries to exchange on the topic of pharmacology, pharmacochemistry, natural drugs, and functional foods (IPIM, 2021); the articles initiatively linked to this conference was collected and published in *Frontiers in Pharmacology* (Zhang, Dias & Lopes, 2021).

Conclusion

The establishment of the GBA provides the region with multi-discipline opportunities. The GBA allows sharing of educational and research resources and promoting academic exchange within the region, nurturing competitive, high-end talents to fulfill the job market in this fast-growing region. With the current high quality medical services in the GBA and the rapidly expanding pharmaceutical and medical device industries, there is high demand for medical devices and pharmaceutical products, particularly in proprietary Chinese medicine. Thus, the development of the two industries in the GBA plays a crucial role in the economic development of the region.

The regulatory, legislation and administration systems of Hong Kong and Macao are different from that of Guangdong Province due to historical background of the two SARs. The GBA can resolve the current situation and encourage trade and collaboration within the region, creating synergistic effects. Macao's successful story of transforming a pure compound from TCM into a product that faces the global market, is a perfect demonstration of the potential TCM development and popularization worldwide. This proves the capability of the region to drive pharmaceutical and economic development with innovation. The GBA is a catalyst for development and economic growth, improving people's life quality in the region.

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