NEW DIETARY INGREDIENT NOTIFICATION FOR UNRIPE JUJUBE FRUIT EXTRACT POWDER

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SECTION A – ADMINISTRATIVE INFORMATION

A.1 Description of the New Dietary Ingredient

The proposed new dietary ingredient (NDI) manufactured by TCI Co., Ltd ("TCI") is Unripe Jujube Fruit Extract powder (hereinafter "Jujube Fruit Extract powder"). The ingredient is prepared as the aqueous extract of unripe fruit from the *Ziziphus mauritiana* Lam. plant, formulated with maize-derived maltodextrin. Fresh unripe jujube fruit has taut green skin that becomes wrinkly and red or maroon as it ripens. The edible fruit from *Z. mauritiana* is known by a wide range of names, such as "Indian jujube," "Chinese date," "masau," "coolie plum," "phutsaa," "tao," "ponsigué," or "ber," among many others, due to its ubiquitous presence in the diet of individuals from various distinct cultures and geographical regions.

The term "dietary supplement" is defined in Title 21 of the *United States Code* (U.S.C.) 321 (ff) (U.S. FDA, 2023) as, among other things:

> [...] *a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients: (A) a vitamin; (B) a mineral; (C) an herb or other botanical; (D) an amino acid; (E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or (F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E).*

This jujube fruit extract powder therefore qualifies as a dietary ingredient that may be lawfully used in dietary supplements, in accordance with 21 U.S.C. 321 (ff)(1)(E) (U.S. FDA, 2023). Specifically, it falls under categories (C) and (F) as an extract of a botanical.

A.2 Description of the Dietary Supplement Product Containing the New Dietary Ingredient

TCI is the bulk ingredient manufacturer of Jujube Fruit Extract powder. The ingredient is intended to be used in dietary supplement products. The general composition of the Jujube Fruit Extract powder is summarized in Table A.2-1 below. (b) (4)

Table A.2-1 General Composition of Jujube Fruit Extract Powder [CONFIDENTIAL]

(b) (4)

A.3 Identification of Trade Secret Information

The following information and their location(s) within the dossier, as indicated in Table A.3-1, are identified as confidential trade secret and/or confidential commercial information under Title 21 of the *Code of Federal Regulations* (CFR) §20.61(d) and 190.6(e) (U.S. FDA, 2022b,c). TCI understands that this information will be kept confidential for 90 days after the filing date of this Notice; however, TCI respectfully requests that certain information, as described in Table A.3-1 below, be kept confidential even after the 90-day date. The confidential and proprietary information is related to Jujube Fruit Extract powder's chemical composition, manufacturing, specifications, certificates of analysis and test methods, and unpublished product-specific safety data.

Table A.3-1 Confidential Chapters and Sections of the New Dietary Ingredient Notification

Confidential Chapters and Sections	Explanation
Sections A.2, B.1, and B.2, and Appendix A – Description of the NDI and manufacturing information	Trade Secret under 21 CFR §20.61(a) (U.S. FDA, 2022b); Sections A.2, B.1, B.2, and Appendix A contain the exact compositional breakdown, raw materials, supplier information, manufacturing process, process controls, and schematic overview of the manufacturing process for TCI's Jujube Fruit Extract powder that must be kept confidential. The information is proprietary and commercially valuable. Confidential Commercial Information under 21 CFR §20.61(b) (U.S. FDA, 2022b); Sections B.1 and B.2 contain confidential information used in TCI's business and this information is customarily held in strict confidence or regarded as privileged. Disclosure of this information would allow competitors to copy TCI's NDI and would likely cause substantial harm to TCI's competitive position.
Sections B.3, B.4, and B.5, and Appendices B, C, and D–Regarding the product specifications and chemical analyses of the NDI	Trade Secret under 21 CFR §20.61(a) (U.S. FDA, 2022b); Sections B.3, B.4, B.5, and the associated data in the appendices contain TCI's product specifications, certificates of analyses, methods of analysis, and additional characterization of the NDI that must be kept confidential because the information is proprietary and commercially valuable. Product specifications and certificates of analysis contain trade secret compositional information. Confidential Commercial Information under 21 CFR §20.61(b) (U.S. FDA, 2022b); Sections B.3, B.4, B.5, and the associated appendices contain confidential information used in TCI's business and this information is customarily held in strict confidence or regarded as privileged. Disclosure of this information would allow competitors to copy TCI's NDI and would likely cause substantial harm to TCI's competitive position.
Sections C.1, C.3.1, and C.4, and Appendices E and F– Comprehensive safety profile, product-specific safety data, and safety narrative	Trade Secret under 21 CFR §20.61(a) (U.S. FDA, 2022b); Sections C.1, C.3.1, C.4, and Appendices E and F contain reference to commercial uses of the NDI and a product-specific study conducted with Jujube Fruit Extract powder. These data are regarded as proprietary information that is not publicly available. Therefore, the information presented in this section is a product of research and innovation that required substantial effort. Accordingly, these sections contain trade secrets and must not be disclosed, as the information is proprietary and commercially valuable. Confidential Commercial Information under 21 CFR §20.61(b) (U.S. FDA, 2022b); Sections C.1, C.3.1, C.4, and Appendices E and F contain confidential information used in TCI's business and this information is customarily held in strict confidence or regarded as privileged. Disclosure is likely to cause substantial harm to TCI's competitive position.

CFR = *Code of Federal Regulations*; NDI = new dietary ingredient; TCI = TCI Co., Ltd.

SECTION B – CHEMISTRY AND IDENTITY

B.1 Description of the New Dietary Ingredient [CONFIDENTIAL]

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Table B.1-1 General Composition of Jujube Fruit Extract Powder [CONFIDENTIAL]

(b) (4)

B.2 Manufacturing Information [CONFIDENTIAL]

B.2.1 Raw Materials

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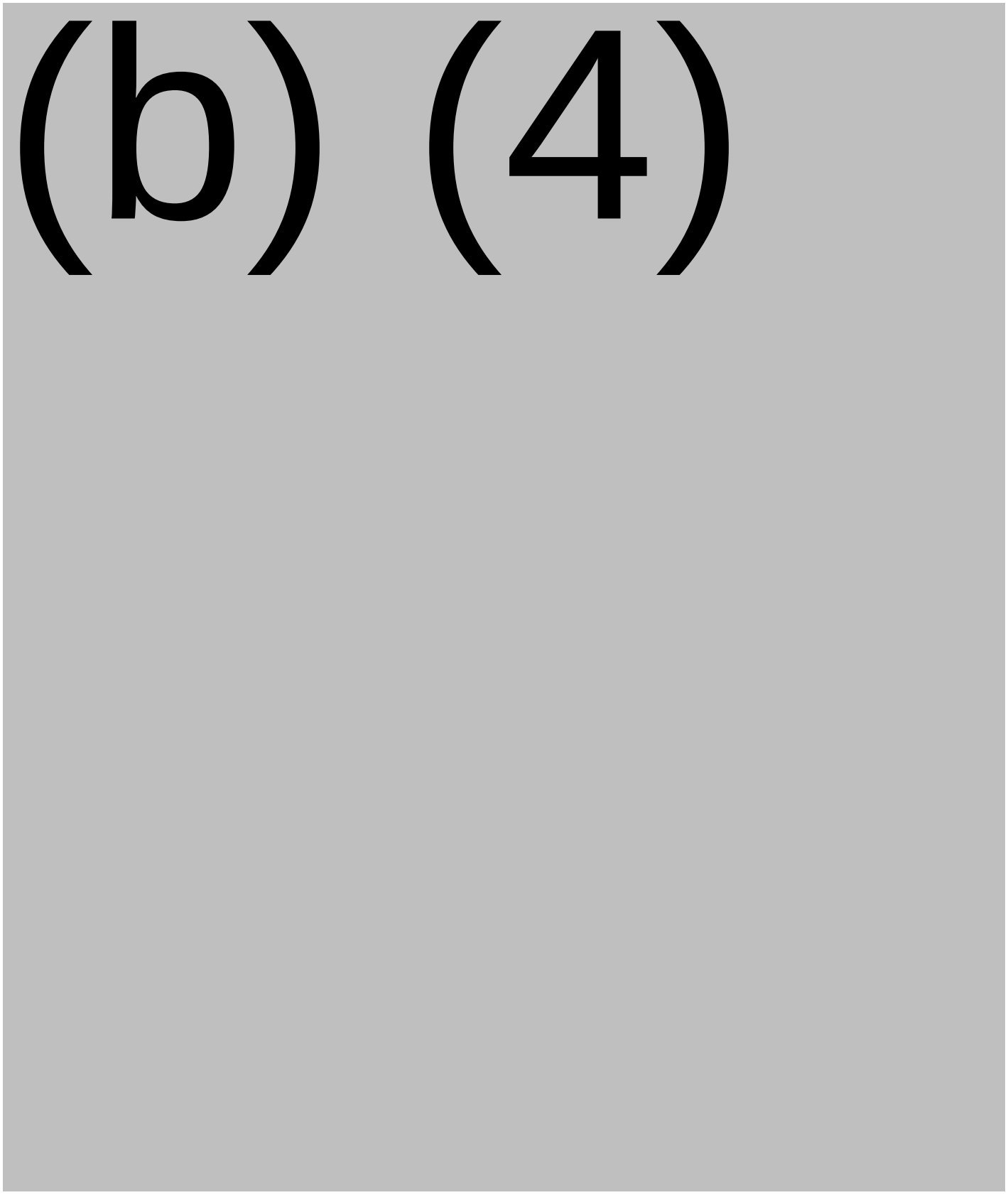
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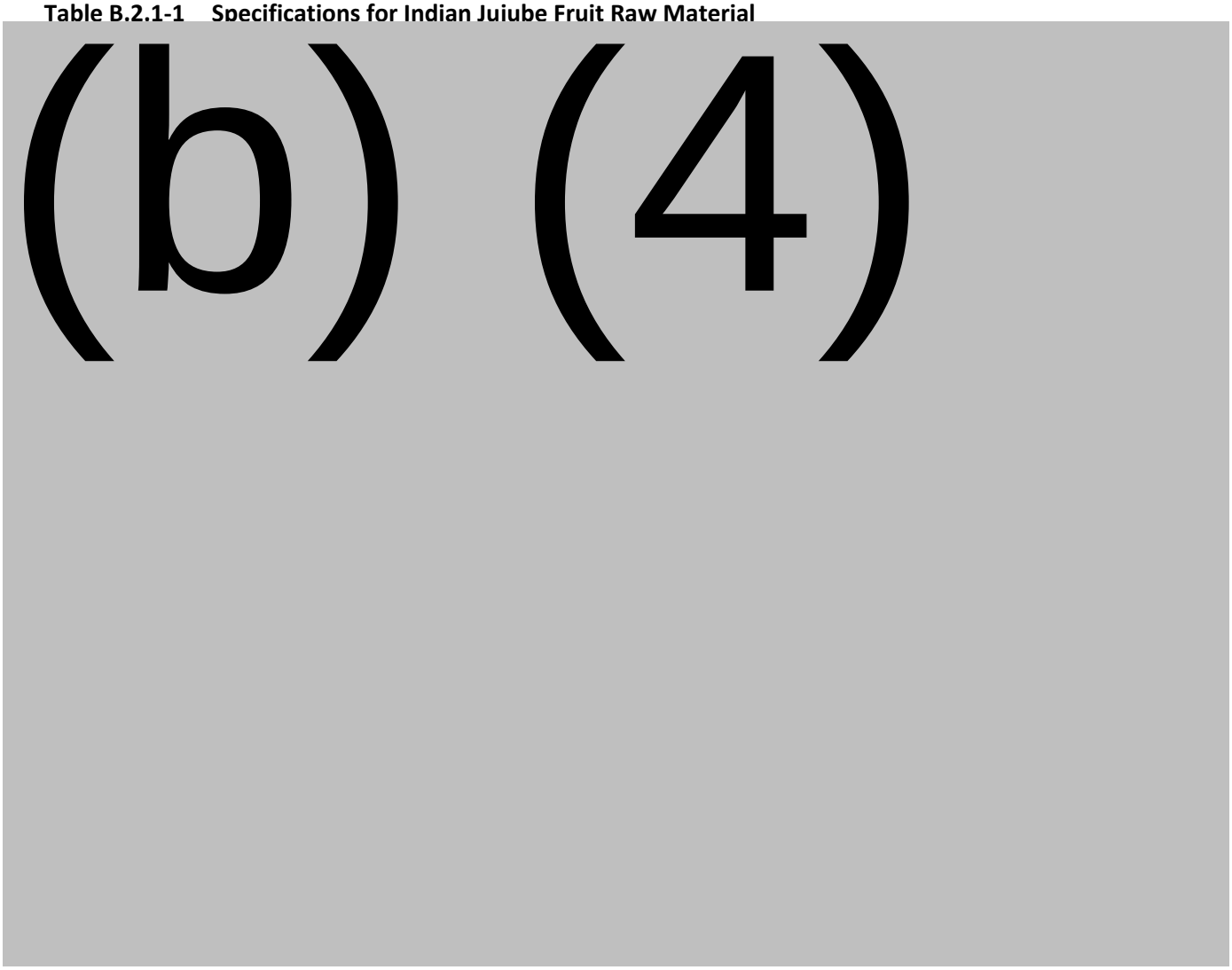
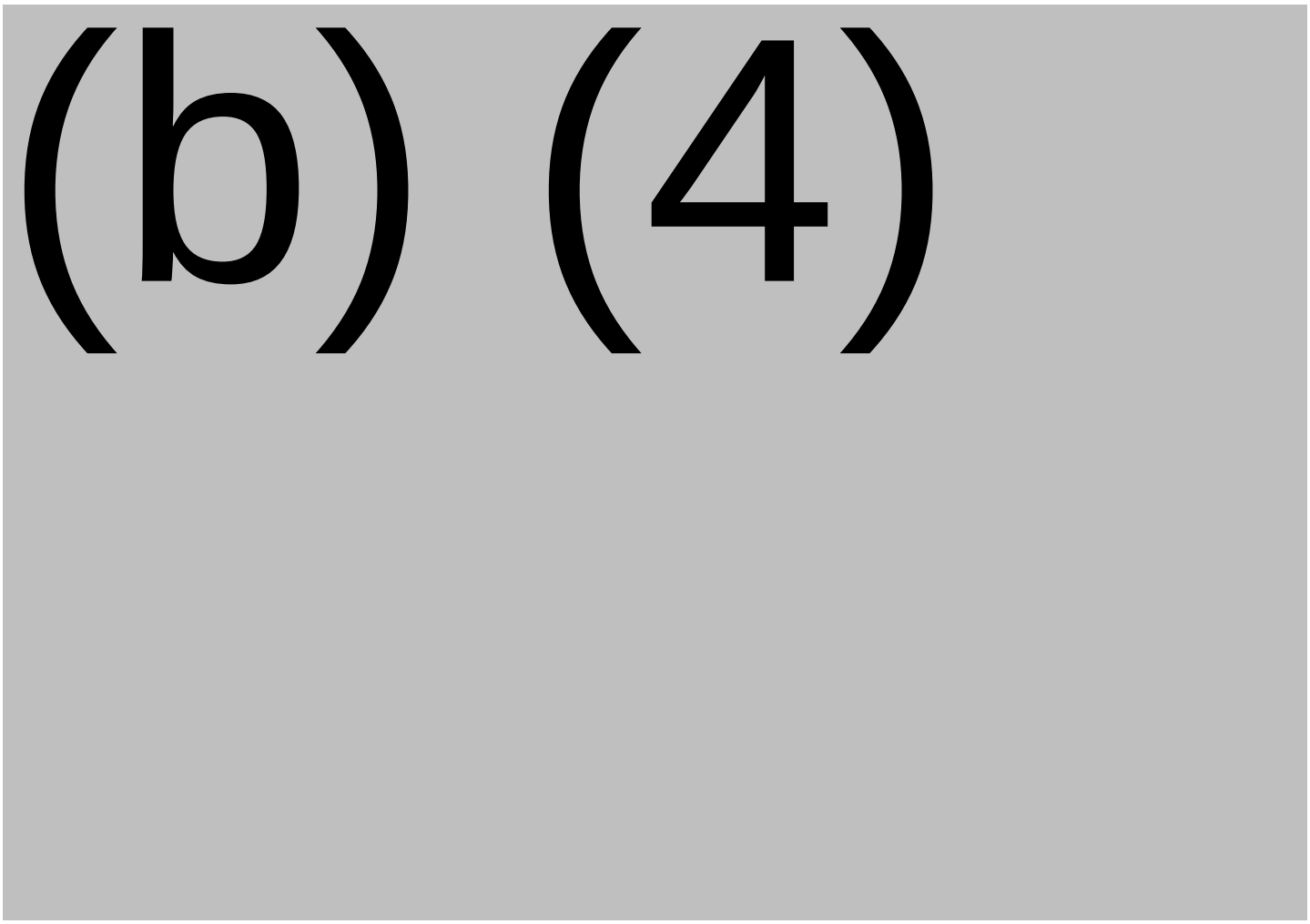
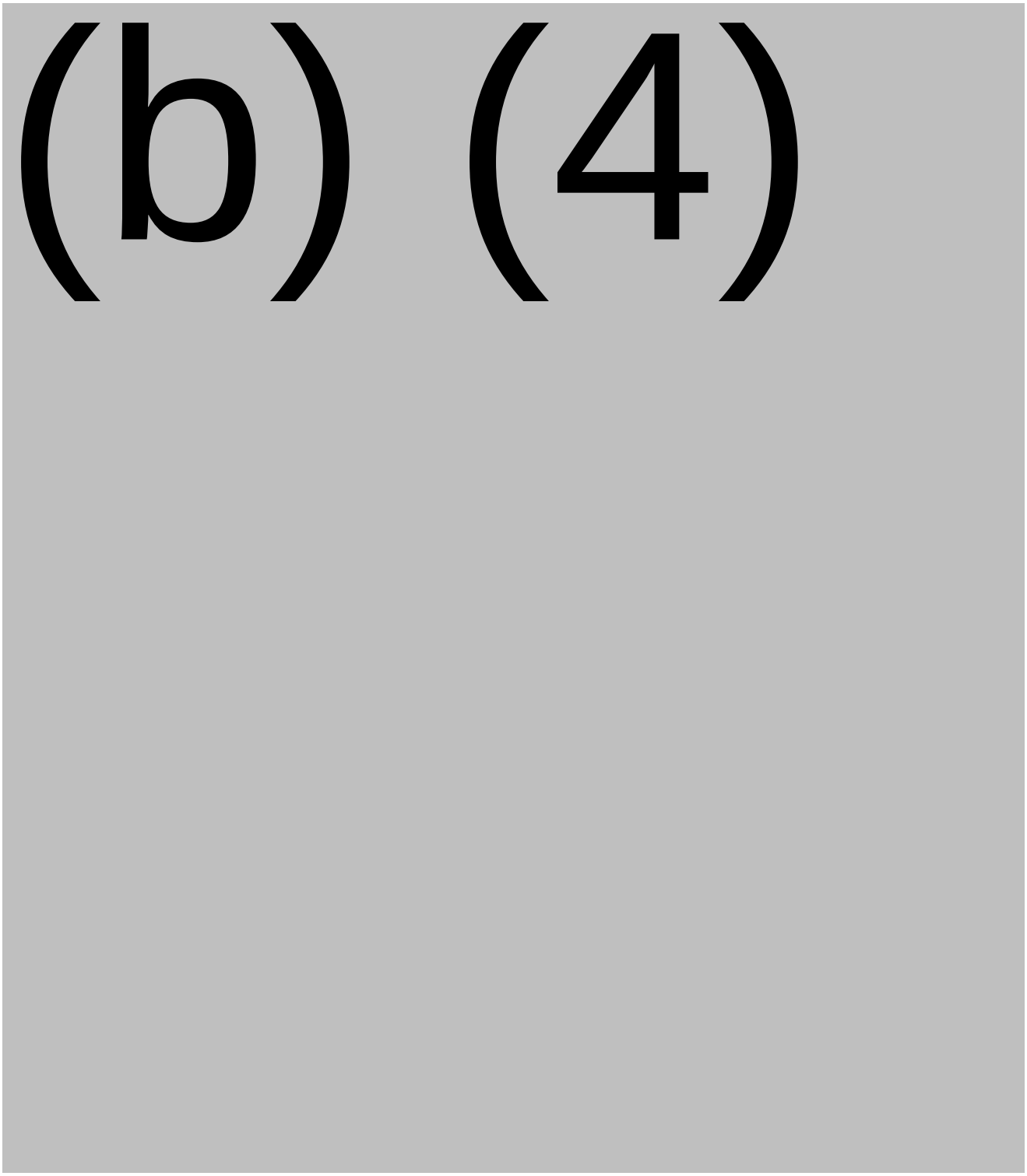
Table B.2.1-1 Specifications for Indian Jujube Fruit Raw Material



B.2.2 Manufacturing Process

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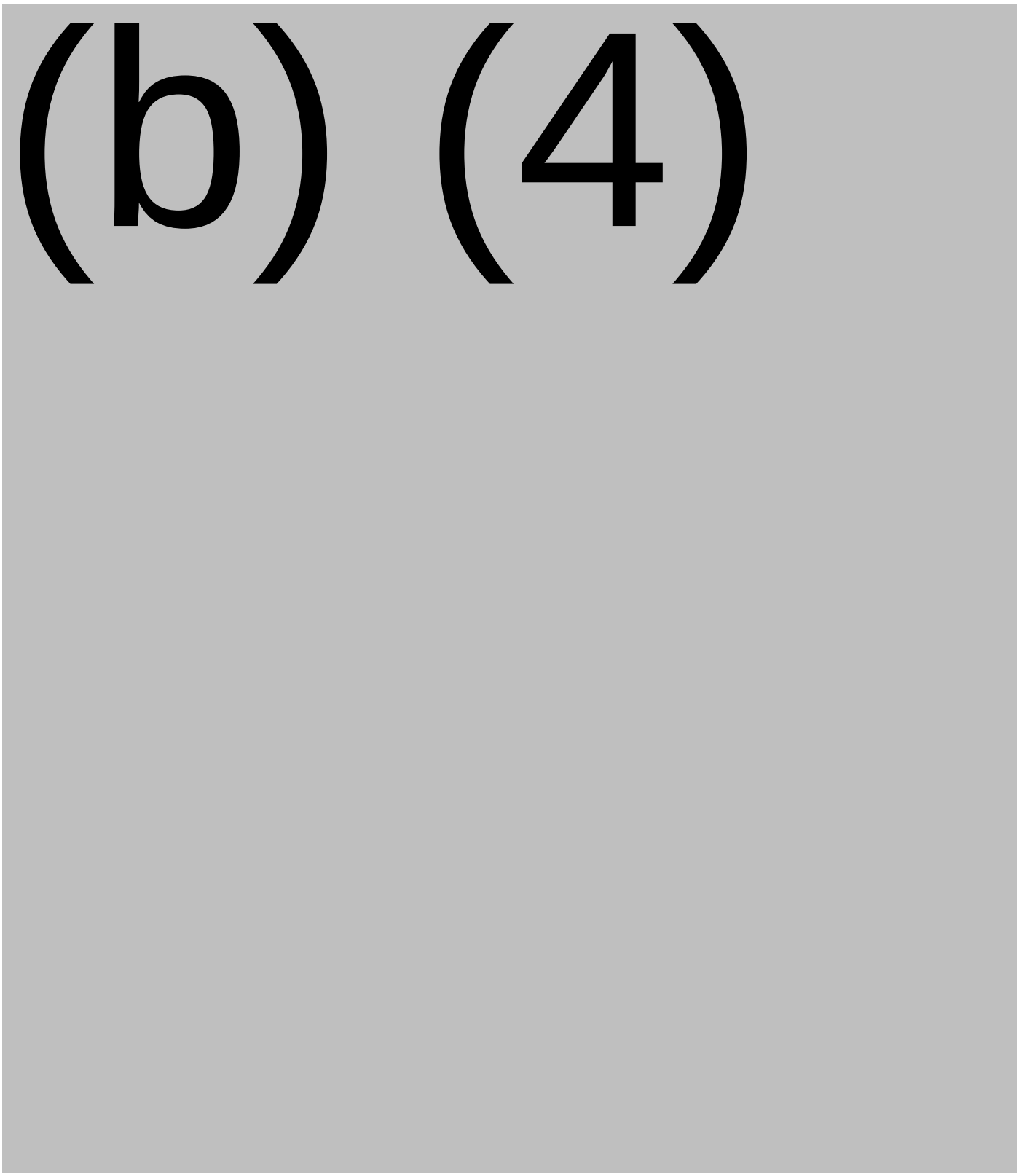
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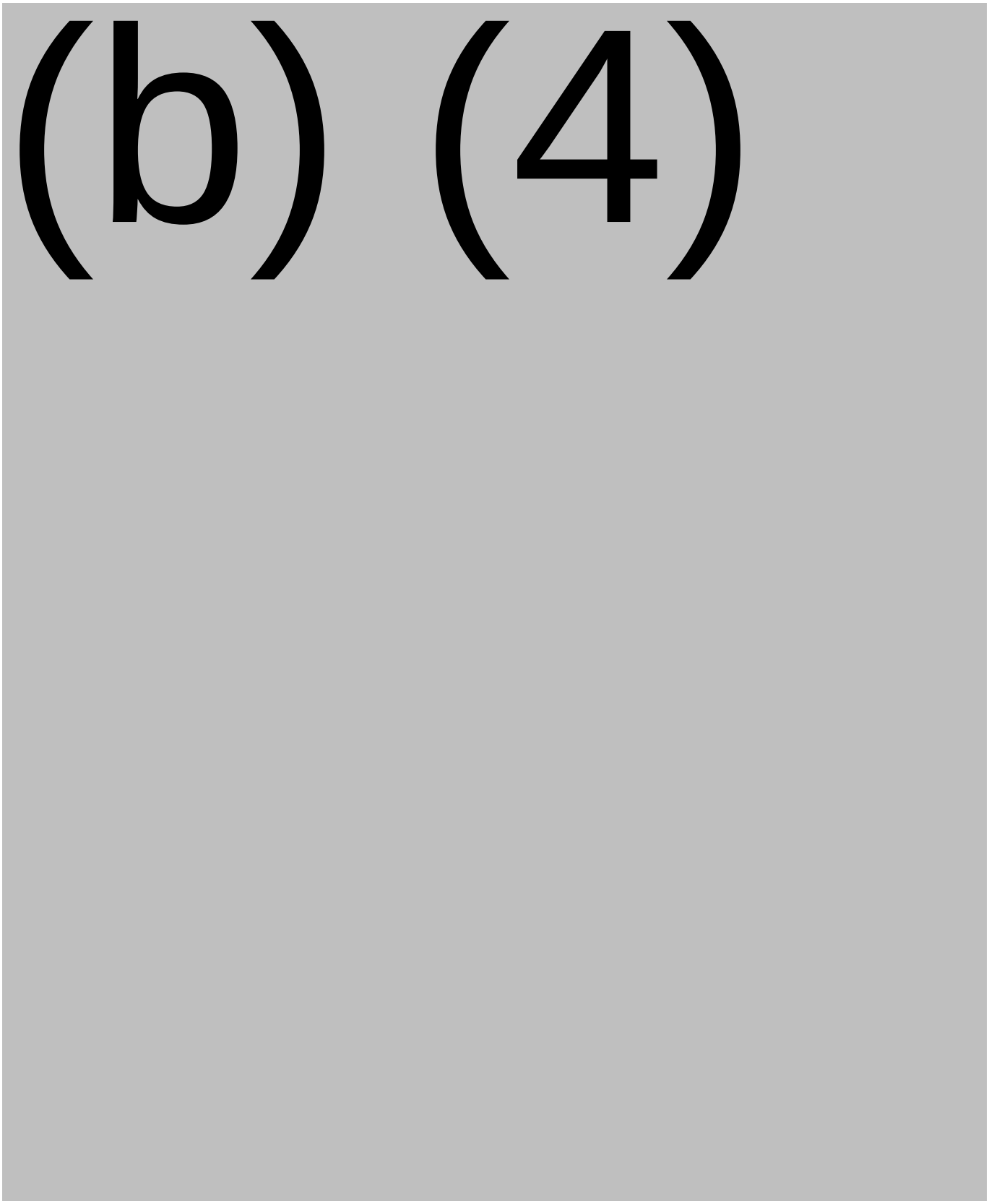
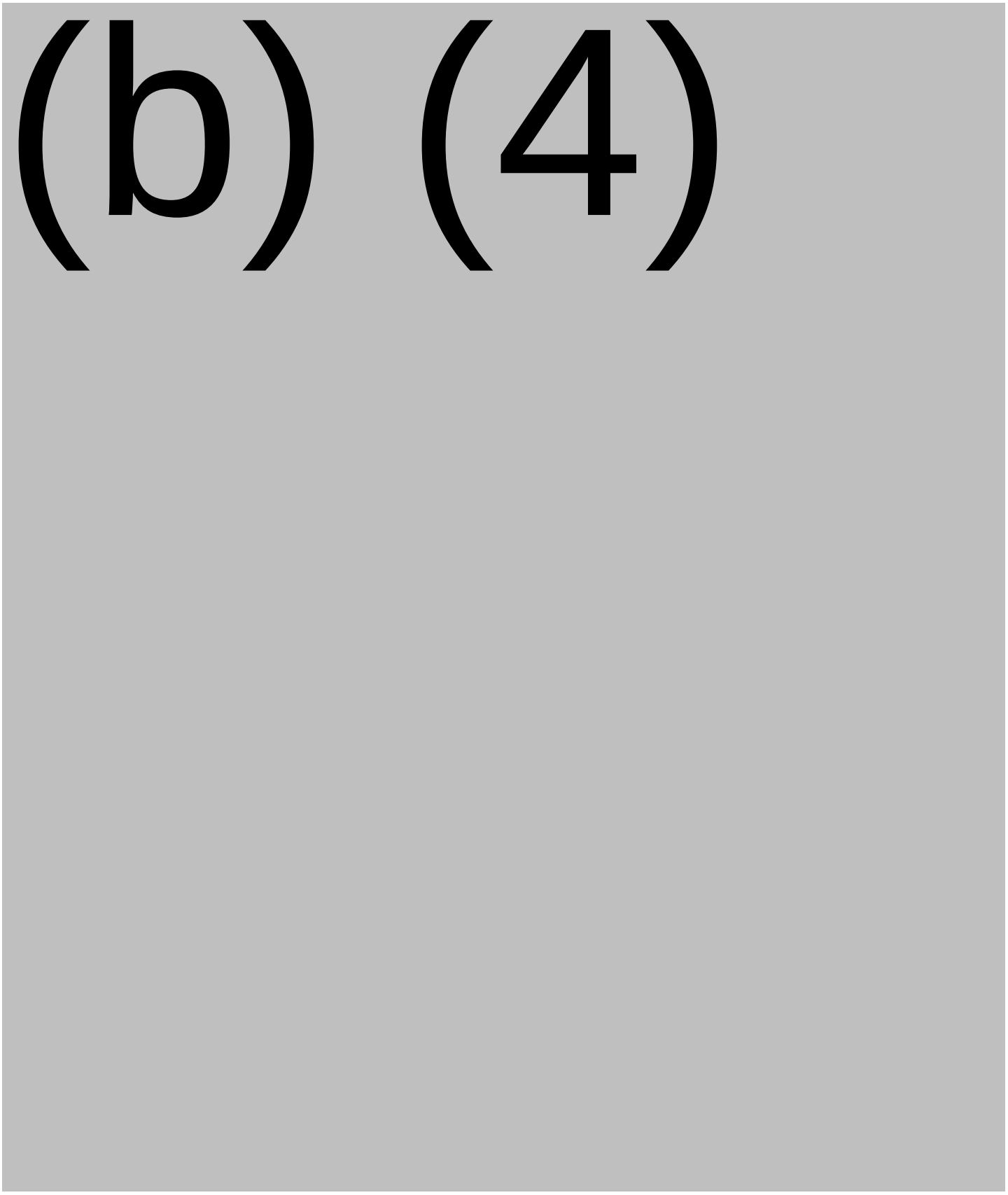
B.3 Product Specifications [CONFIDENTIAL]



B.4 Product Analysis [CONFIDENTIAL]



B.5 Additional Product Characterization [CONFIDENTIAL]

(b) (4)

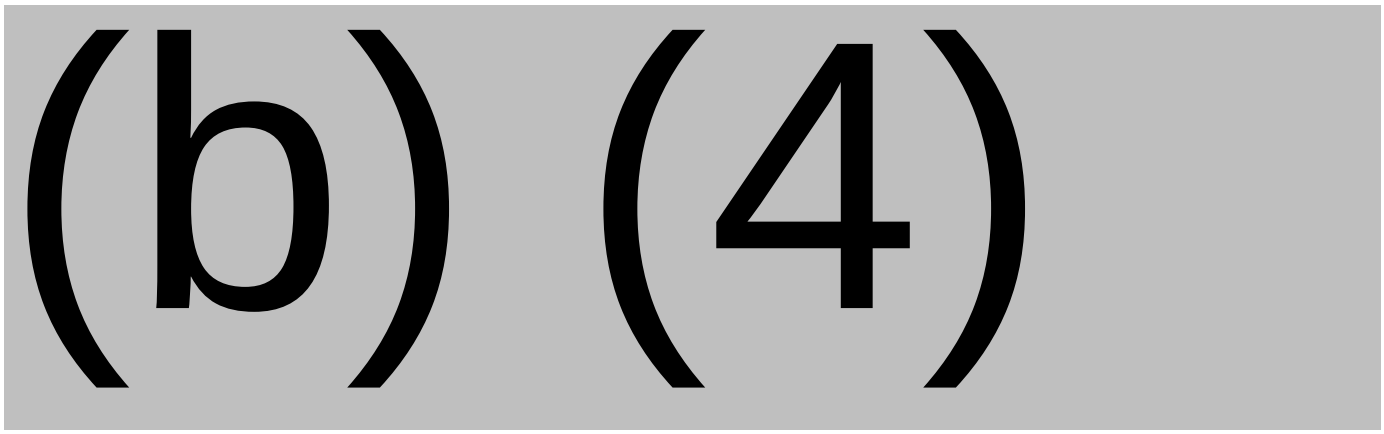
SECTION C – SAFETY AND TOXICOLOGY

C.1 Comprehensive Safety Profile for the New Dietary Ingredient

(b) (4)

Jujubes from *Z. mauritiana* (*i.e.*, Indian jujube fruit) are a well-characterized and widely distributed fruit commonly found in a wide range of tropical and subtropical regions, with a long-established safe history of use in the human diet (see Section C.2.1). Primarily cultivated in arid regions, Indian jujubes are generally consumed raw in India and Southeast Asia; however, the fruit is also dried, boiled, stewed, baked, pickled, or prepared into cakes, alcoholic beverages, or jams and chutneys (Pareek, 2001; Azam-Ali *et al.*, 2006). Globally, it is considered an underutilized crop with significant potential for commercial development and is viewed as extremely valuable for establishing food security due to the heat- and drought-tolerance of the *Z. mauritiana* tree (Arndt *et al.*, 2000; Razi *et al.*, 2013; Maruza *et al.*, 2017; Amin *et al.*, 2018). The fruit of the *Z. mauritiana* plant (both ripe and unripe) is regularly consumed on its own; however, it is also common for the fruit to be pickled, candied, or used in the preparation of butters, beverages (alcoholic and non-alcoholic), cakes, chutneys, fruit snacks, frying oils, jams, salsas, sauces, spiced desserts, and other sweet fruit condiments (Azam-Ali *et al.*, 2006; Dairou *et al.*, 2014; Kavitha *et al.*, 2014; Zozio *et al.,* 2015; Delfanian, 2016; Mateen and Phanikumar, 2018). Based on use levels published in the scientific literature, and reference amounts customarily consumed for each of the noted food uses (*e.g.*, raw fruits, fruits for young children, chutneys, relishes, *etc.*) in the United States (U.S.), typical serving sizes of Indian jujube fruit range from 15 to 125 g/occasion (Dairou *et al.*,2014; U.S. FDA, 2018). Currently, the Taiwan Food and Drug Administration (TFDA) lists Indian dates (*i.e.*, *Z. mauritiana* fruit) as a raw material for use in food and further categorizes them as being available for direct consumption (TFDA, 2017).

(b) (4)



The scientific evidence presented below supports a conclusion that the NDI is "*reasonably expected to be safe*" under the conditions of intended use, which is consistent with the U.S. FDA's position on establishing appropriate margins of safety when establishing the safety of NDIs.

C.2 History of Safe Use

C.2.1 History of Use

Jujubes are the subtropical fruit of flowering plants belonging to the Rhamnaceae family and are often regarded as underutilized crops with significant potential for commercial development (FAO, 2001; Pareek, 2001; Azam-Ali *et al.*, 2006). There are 2 major species of jujube-producing plant widely cultivated for human consumption globally: *Z. mauritiana* Lam. and *Ziziphus jujuba* Mill. (Azam-Ali *et al.*, 2006; Jin, 2018). The fruit from the *Z. mauritiana* plant, also known as "Indian jujube," "Chinese date," "masau," "dunks," "kul," "boroi," "coolie plum," "phutsaa," "tsao," "elantha palam," "ponsigué," or "ber," among many other colloquial names, is known for its mild sub-acid flavor and crisp texture and has been safely consumed as part of the traditional human diet for centuries (Morton, 1987; Pareek, 2001; Nyanga, 2012; Pareek, 2013; Shahrajabian *et al.*, 2019; Chiou *et al.,* 2020; Paul *et al.*, 2021). Notably, it has been reported that scientific studies conducted with *Z. mauritiana* fruit produced in tropical regions often misclassify the fruit as *Ziziphus jujuba*,[1] presumably due to the similarity of appearance shared by the 2 species. There is evidence to indicate that *Z. mauritiana* trees originated somewhere in the northwestern regions of South Asia and that the jujube fruit was frequently consumed by humans as far back as approximately 3,000 to 5,000 years ago (Petrie and Bates, 2017; Suryanarayan *et al*., 2021).

Cultivation of *Z. mauritiana* for human consumption has been documented in numerous tropical and sub-tropical regions of the world across Asia, Europe, the Americas, and Africa, where the fruit is frequently incorporated into the diet (Azam-Ali *et al.*, 2006; Memon *et al*., 2013; Palejkar *et al.*, 2012; Pareek, 2013; Al-Saif *et al.*, 2021). The tree is also sporadically distributed across Australia, where the fruit is known as the "Chinee Apple" and is known to be edible (ALA, 2023). In arid regions, *Z. mauritiana* trees are considered extremely valuable for establishing food security due to their drought resistance and tolerance for very high temperatures (Arndt *et al.*, 2000; Razi *et al.*, 2013; Maruza *et al.*, 2017; Amin *et al.*, 2018; Muhammad *et al.*, 2022). In Southeast Asia, it is common for unripe jujube fruit to be consumed with salt, whereas in India, it is mostly the fresh ripe fruit that is consumed raw (Azam-Ali *et al.*, 2006). The fruit of *Z. mauritiana* can vary in size with cultivar; however, the edible flesh of the fruit has been observed to range from 4.61 to 36.67 g/fruit with a mean of 17.17 g/fruit (Abdel-Sattar *et al.*, 2021). In Zimbabwe, fresh jujube fruit constitutes a significant portion of the human diet from June to September while the fruit is considered to

[1] https://uses.plantnet-project.org/en/Ziziphus_mauritiana.

be “in season” and is otherwise consumed in a dehydrated form throughout the remaining months of the year (Azam-Ali *et al.*, 2006). In a survey of 50 random households from 3 districts in Zimbabwe, 96% of the households indicated that they consume the fresh fruit (as “masau”) daily throughout the harvest season (Nyanga *et al.*, 2013). While the fruit of *Z. mauritiana* is frequently consumed fresh or dried, boiling, stewing, and baking are also often used to prepare the fruit (Pareek, 2001).

Common culinary uses of Indian jujube fruit reported in the literature include pickling, candying, and preparation of jams, beverages, butters, and cheese-like pastes (Morton, 1987; Pareek, 2001; Siriamornpun *et al.*, 2015; Zozio *et al.*, 2015; Dalal *et al.*, 2019; Mathangi and Maran, 2020; Sharif *et al.*, 2022). There are numerous examples of *Z. mauritiana* fruit being used to prepare jam, either utilizing slightly unripe fruit (Azam-Ali *et al.*, 2006) or more mature fruit (Azam-Ali *et al.*, 2006; Mateen and Phanikumar, 2018). It is also common for the fruit to be processed into a variety of alcoholic beverages, including African wines, “Crema de ponsigue” in Venezuela, and “Kachasu” in Zimbabwe and Malawi (Azam-Ali *et al.*, 2006; Nyanga *et al.*, 2008; Lim, 2012), and non-alcoholic beverages (Azam-Ali *et al.*, 2006; Kavitha *et al.*, 2014).
Ziziphus mauritiana fruit is also often used in the preparation of cakes. In Western Sudan and Zambia, the dried and fermented pulp of *Z. mauritiana* fruit is pressed into cakes that have been likened to gingerbread (Azam-Ali *et al.*, 2006). In Cameroon, *Z. mauritiana* fruit (as “Jaabi”) is processed into small round cakes called “Yaabande” with each individual cake piece containing 40 to 70 g of *Z. mauritiana* fruit (Dairou *et al.*, 2014) and in Guadeloupe, the fruit (as “pommesurette”) is processed into nutritious jujube cakes (Zozio *et al.*, 2015). In Niger and Mali, the fruit is used to produce flours for traditional loaves and flatbreads (Williams, 1998; Azam-Ali *et al.*, 2006). Finally, a brief search of the internet indicates widespread use of Indian jujube fruit as an ingredient in various beverages,[2,3] spiced desserts,[4] sauces, chutneys, salsas,[5] fruit snacks,[6] and other sweet fruit condiments such as “Ber Ka Achar.[7]” Typical serving sizes for such food uses can vary; however, it can be reasonably expected that regular daily consumption of *Z. mauritiana* fruit (including both ripe and unripe fruit) would range from 15 to 125 g/serving based on reference amounts customarily for each of these uses consumed in the U.S. (U.S. FDA, 2018). Reported daily use of jujube fruit in many jurisdictions therefore far exceeds (approximately 60- to 500-fold for individual food uses) the 0.25 g/day jujube fruit extract that can be expected from consumption of TCI’s Jujube Fruit Extract powder as described herein.

Due to its global popularity as a food, many studies have been conducted to evaluate the proximate composition, mineral and phytochemical content, and functional activities of fruit from *Z. mauritiana* (Azam-Ali *et al.*, 2006; Dureja and Dhimon, 2012; Memon *et al.*, 2012; Krishna and Parashar, 2013; Nyanga *et al.*, 2013; Pareek, 2013; Kavitha *et al.*, 2014; Amin *et al.*, 2018; Kushwada *et al.*, 2019; Hasan *et al.*, 2022). Several studies have also been conducted to examine the genetic diversity of *Z. mauritiana* cultivars and the presence of desirable fruit properties such as fruit mass and yield in different cultivars (Amin *et al.*, 2018; Chiou *et al.*, 2020). The high ascorbic acid content and antioxidant activity of *Z. mauritiana* fruit has rendered it an appealing “healthy” option for human consumption (Shams and Wadhawan, 2019; Hasan *et al.*, 2022). As such, individuals from many different regions where Indian jujubes are plentiful will also readily use the *Z. mauritiana* fruit (or various preparations such as beverages and decoctions) for its perceived efficacy in improving digestion and various other ailments caused by oxidative stress (Azam-Ali *et al.* 2006; Lim, 2012; Kaur *et al*., 2015; Shams and Wadhawan, 2019; Alsayari and Wahab, 2021; Prakash

[2] https://www.winemag.com/2021/03/01/masau-wine-zimbabwe-recipe/.
[3] https://www.tarladalal.com/grapefruit-indian-jujube-infused-water-41841r.
[4] https://recipebook.io/home/recipedetails/rbk_5c51c019798fe/indian-jujube-refresher.
[5] http://www.thesecretingredient.in/green-ber-ki-chutney-indian-plum-mint-dip-smooth-minty-jujube-salsa/.
[6] https://southindianfoods.in/elantha-vadai-jujube-vada-recipe.html.
[7] https://crispandcurry.com/easy-ber-indian-jujube-recipes/.

et al., 2021). Traditional use of antioxidant-rich fruits such as Indian jujube is particularly commonplace, due to their perceived pharmacological value in folk medicine.

A ready-to-serve (RTS) beverage produced from *Z. mauritiana* fruit was compared with the raw, unprocessed fruit in a study of physicochemical and antioxidant properties (Kavitha *et al.*, 2014). The ripe fruit were cleaned, destoned, and diced before boiling in water at a 1:1 ratio for 20 to 30 minutes. Sugar and citric acid were then added before filtration and bottling. Similarly, in a study of product development and shelf life, a RTS carbonated *Z. mauritiana* fruit beverage was prepared from 5 kg of destoned and diced *Z. mauritiana* fruit, boiled in water at a 1:1 ratio for 20 minutes then blended, sieved, and mixed with sugar to prepare a syrup (2,625 mL) (Shams and Wadhawan, 2019). The syrup (80 mL) was then added to 170 mL of carbonated water to prepare the final RTS beverage. Five kilograms of raw jujube fruit were used to produce approximately thirty-two 250-mL bottles of carbonated beverage (2,625 mL syrup/80 mL syrup/bottle = 32.8 bottles), each one containing the equivalent of approximately 156 g of concentrated *Z. mauritiana* fruit juice (5 kg of fruit/32 bottles = 0.156 kg of fruit/bottle).

In a study conducted by Delfanian *et al.* (2016) on jujube fruit extract as a functional food, the effect of various extraction methods (*i.e.*, ultrasound-assisted, supercritical CO_2, and solvent) on the antioxidant activity of *Z. mauritiana* fruit extracts and their function as natural antioxidants in frying oils was evaluated. Raw Iranian jujube fruit were harvested, sun-dried, powdered to 40-mesh, and extracted for 48 hours before being concentrated with a rotary evaporator at 50°C. Water, ethanol, and ethanol-water were all evaluated as extraction solvents. Three samples were evaluated for each extraction solvent: standard solvent extraction, ultrasound-assisted extraction, and supercritical CO_2 extraction. The total phenolic content of the extracts ranged from 285.74 to 664.72 mg of gallic acid equivalents (GAE)/g. The greatest extraction yield and total phenolic content were observed in ultrasound-assisted water and ethanol-water extracts; however, only the ethanol-water form was further evaluated in the frying oil tests since it had slightly higher antioxidant levels. To evaluate its effects on total polar compound production (a major oil degradation indicator) during frying of soybean frying oil, the jujube fruit extract was added to soybean oil at either 600 ppm or 800 ppm for comparison against common industry synthetic antioxidants (*i.e.*, butylated hydroxytoluene, butylated hydroxyanisole, and tertiary butylhydroquinone), which are often used to increase oxidation stability and shelf life of oil products. Each of the soybean oil preparations were heated at 185°C for 24 hours and used to fry 20-g batches of potato pieces for 7 minutes. Oil samples were collected after time of heating (0, 4, 8, 12, 16, 20, and 24 hours) and tested for total polar compounds. The oxidation rates of the frying oils were lowest in samples containing jujube fruit extract. These findings indicate that jujube fruit extracts could be used to produce an antioxidant effect when present in frying oils for food production at levels up to 800 ppm.

In another study, mixed jam formulations containing *Z. mauritiana*fruit (as “ber”) and kiwi fruit were evaluated in a study for sensory characteristics and other compositional parameters, such as polyphenolic content and antioxidant activity (Mateen and Phanikumar, 2018). Nine different jam preparations containing various combinations of kiwi and ber fruits were evaluated. The ber fruit was cut into pieces following harvest, grinded, and lyophilized prior to jam formulation, with each jam formulation containing ber fruit at levels ranging from 5 to 15 g/100 g. A sensory panel of 20 adults (12 men, 8 women) evaluated each jam formulation for appearance/color, taste, consistency/texture, aroma, and overall acceptability, and identified a formulation containing 15 g of ber fruit/100 g as the most acceptable. Additionally, jam formulations containing increased levels of ber fruit were observed to also have increased total phenolics and antioxidant capacity relative to formulations that contained less ber. The authors therefore concluded that ber fruit has a positive effect on the jam quality and could be utilized to improve the nutritional value of foods by increasing antioxidant capacity and total phenolic content.

The effect of Indian jujube fruit maturity on the nutritional value (as measured by vitamin C and total phenolic content, as well as antioxidant capacity) of traditional African jujube fruit cakes was evaluated in a study conducted by Zozio *et al.* (2015). Indian jujube fruit (known as "pommesurette" in Guadeloupe) at 2 different stages of maturity ("medium" and "most" ripe) were dried, ground, and cooked into cakes that each contained 13 g of jujube flour. The cakes were prepared by first drying the de-stoned fruit (45°C for 30 hours), grinding and powdering the fruit to a jujube flour (size grading 465 µm), and cooking (10 minutes for 100°C in a steam oven). Vitamin C and total phenolic content, as well as antioxidant capacity were evaluated in the raw fruit material, and the flours and cakes were prepared from each stage of fruit maturity. Cakes prepared from medium-ripe fruit were observed to contain significantly greater vitamin C and total phenolic content as well as greater antioxidant capacity than the cakes prepared from more mature fruits. The authors thus strongly recommended the use of jujube fruit in general food applications due to the increased nutritional qualities they observed in cakes prepared from medium-maturity fruit.

C.2.2 Current Regulatory Status

The U.S. Department of Agriculture includes raw jujube (*Z. jujuba*) and fresh or dried Chinese jujube in the Standard Reference Legacy list of foods (USDA, 2019a,b). While *Z. jujuba* and *Z. mauritiana* are distinct plant species, the fruits are compositionally similar and often discussed in similar context as far as food uses (Pareek, 2013; Rashwan *et al.*, 2020). The NDI discussed herein, TCI's Jujube Fruit Extract powder, is produced *via* water extraction of the raw unripe fruit from *Z. mauritiana*. Water is an approved extractant for food production in the U.S., and this manufacturing process does not include any separation or purification steps beyond what is required to remove excess water from the final product.

Internationally, the TFDA currently permits the use of Indian dates (*i.e.*, *Z. mauritiana* fruit) as a raw material for use in food and further categorizes them as being available for direct consumption in Taiwan (TFDA, 2017). Since 2018, TCI's Jujube Fruit Extract powder has been marketed in various supplement products at daily use levels of 0.5 g of Jujube Fruit Extract powder/day. Translated product labels (including complete ingredient lists for each supplement product with full compositional itemization and instructions for use), and examples of individual sales orders from 2021, are provided in Appendix E. Specifically, 2 supplement-type products (*i.e.*, "Surei Labo Artichoke Fermented Ginger Complex Drink" and "XGENE Compound Solid Drink") are currently marketed in China and contain 0.25 to 0.5 g of TCI's Jujube Fruit Extract powder per unit and are recommended to be consumed daily. "Surei Labo" is a 50-mL formulated drink product that is to be well shaken before direct consumption, once per day. "XGENE" is marketed as a processed powder mixture, sold in 3-g packets, that is intended to be brewed with 200 mL of water prior to consumption, twice daily. To date, there are no known reports of adverse events occurring from the use of these products as recommended.

The recommended daily use level of TCI's Jujube Fruit Extract powder (*i.e.*, 0.5 g/day), proposed for use as an NDI in the U.S., has therefore been established to align with the historical safe use levels of this ingredient (since 2018) in international supplement products, as described above (Appendix E).

C.3 Studies to Support Safety

C.3.1 Studies Conducted with Jujube Fruit Extract Powder

C.3.2 Studies Corroborative of New Dietary Ingredient Safety

To identify additional information pertinent to the safety of jujube fruit aqueous extract, a literature search was conducted through November 2023 using the search engine ProQuest™ accessing the following databases: Adis Clinical Trials Insight, AGRICOLA, AGRIS, Allied & Complementary Medicine™, BIOSIS® Toxicology, BIOSIS Previews®, CAB ABSTRACTS, Embase®, Foodline®: SCIENCE, FSTA®, MEDLINE®, NTIS: National Technical Information Service, Toxfile®; and Toxicology Abstracts. Three studies were identified in the published scientific literature that corroborate the safety of Jujube Fruit Extract powder. These studies were conducted with either the fresh juice from unripe *Z. mauritiana* jujube fruit or *Z. mauritiana* aqueous extract test articles, and therefore can support the reasonable expectation of safety of TCI's Jujube Fruit Extract powder. Results from the identified studies are discussed below.

The effect of fresh juice from unripe *Z. mauritiana* jujube fruit in the diet on growth, blood composition, histology, and general toxicological effects was investigated in a 4-week study, wherein 3 groups of male albino CFT rats (8/group) were administered test diets containing either 0 (normal control diet) or 10 mL/day of unripe jujube juice (Padmanabhan *et al.*, 1993). The safety of 2 different unripe jujube fruit juices (prepared from 2 different juice extraction processes, with or without removal of seed) was evaluated, which were administered in 2 distinct treatment groups. Body weights, feed consumption, clinical chemistries (serum glucose, proteins, albumin, cholesterol, serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, and alkaline phosphatase), and hematology (hemoglobin, erythrocytes, leucocytes, and packed cell volume) were monitored as part of this study. Histopathological examination of the organs (*e.g.*, liver, kidney, stomach, spleen, heart, and lungs) was performed upon study termination. The measured feed consumption within this study indicated consumption of 5 to 8 mL/day of unripe jujube fruit juice throughout the study, which the authors suggested is comparable to consumption of 2 to 3 L/day in a 60-kg human. It is not explicitly stated how the authors made this equivalence; however, the authors presumably utilized a 0.15-kg body weight for the treated rats (which aligns with the measured body weights for animals included in this study) and a juice density of 1 g/mL in the calculations. As such, the 5 to 8 mL/day actual consumption of unripe jujube juice correlates to approximately 5,000 to 8,000 mg/day (or 33,333 to 50,000 mg/kg body weight/day). No adverse effects were identified in any of the measured parameters. Based on these results, the authors asserted that juice pressed from unripe *Z. mauritiana* jujube fruit is likely to be of benefit to human consumers.

As part of a study conducted to evaluate the effect of "high doses" of Iranian jujube on biochemical and hematological parameters in rats, Safizadeh *et al*. (2016) administered groups of healthy male Wistar rats (7/group) either 0, 150, 500, 1,000, 2,000, or 5,000 mg of jujube extract/kg body weight/day *via* gavage for 14 days. The extract test article used in this study was prepared by subjecting 5 g of dried jujube fruit to extraction in 100 mL of boiling water for 2 hours, followed by freeze drying. Test animal body weights were measured at the beginning and end of the dosing period, and blood samples were collected upon study completion. Hematological analysis was conducted to measure red blood cells, hemoglobin, packed cell volume, total white blood cells, leukocyte count, and thrombocyte count. Biochemical analyses were conducted on fasting blood sugar, lipid profile (cholesterol, triglyceride, low-density lipoprotein, high-density lipoprotein), total protein, albumin, and total bilirubin. Various additional parameters were also monitored as an assessment of liver function (*i.e.*, ALT, AST, alkaline phosphatase, and lactate dehydrogenase) or kidney function (*i.e.*, BUN, CRE, and uric acid). No changes in body weight, hematological and biochemical parameters, or mortality were observed in any of the Jujube treatment groups. Small but significant increases in each of the liver enzymes were observed in rats administered doses of ≥2,000 mg of jujube fruit extract/kg body weight/day. Significant increases in BUN, CRE, and uric acid were also noted in rats administered 5,000 mg of jujube fruit extract/kg body weight/day. While the study authors concluded that administration of 5,000 mg of aqueous jujube fruit extract/kg body weight/day did not result in hepato- or nephro-toxicity in rats over the 14-day period, a more conservative no-observed-adverse-effect level (NOAEL) of 1,000 mg/kg body weight/day in rats was chosen for the purposes of this safety assessment.

In another study, conducted primarily to evaluate the antidiabetic activity of various *Z. mauritiana* fruit extracts, a preliminary acute toxicity study was conducted in which groups of 5 healthy female Wistar rats were provided single oral doses (2,000 mg/kg body weight) of crude aqueous jujube fruit extract (25 g of fruit in 200 mL of boiling water for 15 minutes, followed by evaporation) or a range of other fractionated solvent extracts (Jarald *et al.*, 2009). The *Z. mauritiana* fruit used to prepare the test article was harvested in Tamil Nadu, India, where aqueous extracts of *Z. mauritiana* fruit are regularly consumed in traditional herbal preparations. Test animals were monitored for 14 days post-dose for mortality and general behavior, in accordance with Organisation for Economic Co-operation and Development Test Guideline 420 (*Acute Oral Toxicity - Fixed Dose Procedure*). No adverse effects were noted, and the authors concluded that 2,000 mg/kg body weight of crude aqueous jujube fruit extract is safe for oral consumption.

Taking into account the intended use level of 0.5 g of Jujube Fruit Extract powder/day (*i.e.*, 0.25 g of jujube fruit extract/day or 3.57 mg/kg body weight/day in a 70-kg adult human), along with the lowest NOAELs that can be reasonably inferred from the results from these studies (up to 50,000 mg/kg body weight/day for unripe *Z. mauritiana* fruit juice, or 1,000 mg/kg body weight/day for aqueous jujube extracts) (Padmanabhan *et al.*, 1993; Jarald *et al.*, 2009; Safizadeh *et al*., 2016), margins of safety of 14,000 and 280, respectively, were calculated.

C.4 Safety Narrative of the Dietary Supplement

TCI intends to introduce Jujube Fruit Extract powder to the U.S. marketplace as a dietary supplement. The following narrative provides a concise summary of the scientific basis that establishes the use of Jujube Fruit Extract powder as a dietary supplement that is reasonably expected to be safe when used under the conditions described herein.

(b) (4)

The raw material, Indian jujube fruit from *Z. mauritiana*, has a long history of safe use as a food in the human diet in many Asian and African countries, such as India, Pakistan, Afghanistan, Algeria, Egypt, Kenya, Zimbabwe, Malaysia, Japan, Nepal, Australasia, the Philippines, the territory of Pacific Islands, and various other subtropical regions of the globe (Nyanga, 2012; Oshima *et al*., 2014; Prakash *et al.*, 2021). The *Z. mauritiana* tree (sometimes referred to erroneously as "*Ziziphus jujuba*," a distinct species of jujube-bearing fruit tree) bears fruit that is also referred to as Indian plum, Chinese date, ber, or dunks, among an extensive range of other colloquial names, and is commercially farmed for use in foods due to its nutritional composition (richness in ascorbic acid, minerals, and carbohydrates) (FAO, 2001; Azam-Ali *et al.*, 2006; Pareek, 2013; Prakash *et al.*, 2021) and anti-oxidant content (Zozio *et al.*, 2015; Delfanian *et al.*, 2016; Koley *et al*., 2016; Mateen and Phanikumar, 2018; Aldhanhani *et al.*, 2022), or for use in traditional medicines (Morton, 1987; Jarald *et al*., 2009; Shahrajabian *et al.*, 2019). In countries where the wild jujube fruit grows, it is common for the fruit to be consumed fresh daily throughout the harvest season or in a dehydrated form when the fruit is not "in season" (Nyanga *et al.*, 2013).

The ripe and unripe fruit of the *Z. mauritiana* plant are both regularly consumed raw; however, it is also common for the fruit to be pickled, candied, or used in the preparation of butters, beverages (alcoholic and non-alcoholic), cakes, chutneys, fruit snacks, frying oils, jams, salsas, sauces, spiced desserts, and other sweet fruit condiments (see Section C.2.1). Based on the described food uses of this fruit from the scientific literature, and reference amounts customarily consumed for each of the noted food uses (*e.g.*, raw fruits, fruits for young children, chutneys, relishes, *etc.*) in the U.S. (U.S. FDA, 2018), it can be reasonably expected that, globally, typical serving sizes of Indian jujube fruit range from 15 to 125 g per eating occasion (Dairou *et al.*, 2014). These serving sizes, corresponding to regular consumption of individual foods containing *Z. mauritiana* fruit, far exceed (b) (4)

Currently, the TFDA lists Indian dates (*i.e.*, *Z. mauritiana* fruit) as a raw material permitted for use in food and further categorizes them as being available for direct consumption (TFDA, 2017). (b) (4)

(b) (4)

Furthermore, the margin of safety from the proposed recommended use level of TCI's Jujube Fruit Extract powder as an NDI relative to the long history of safe use is (b) (4) as established by regular global dietary consumption of the raw Indian jujube fruit from *Z. mauritiana* (both ripe and unripe) and the documented commercialization of dietary supplement products in China that contain the NDI. The well-established history of *Z. mauritiana* fruit use in the human diet strongly supports a conclusion that the NDI is "*reasonably expected to be safe*" under the conditions of intended use. This conclusion is consistent with the U.S. FDA's position on establishing appropriate margins of safety to establish the safety of NDIs:

> *When the notification relies on a history of safe use, a margin of safety should be calculated based upon the historical levels of the NDI that were safely consumed and the NDI intake levels that would result from the conditions of use proposed in the notification. A margin of safety of one (or less than one) corresponds to the argument that a history of safe use alone is sufficient to demonstrate the safety of the proposed use based on conditions of use that are the same or lower, respectively, than the conditions of historical use.*

In conclusion, the weight of the scientific evidence supports that the use of Jujube Fruit Extract powder as an NDI at levels of up to 0.5 g/day is reasonably expected to be safe.

SECTION D – COMPLETE LIST OF REFERENCES

Abdel-Sattar M, Almutairi KF, Al-Saif AM, Ahmed KA (2021). Fruit properties during the harvest period of eleven Indian jujube (*Ziziphus mauritiana* Lamk.) cultivars. Saudi J Biol Sci 28(6):3424-3432 [plus supplementary table]. DOI:10.1016/j.sjbs.2021.03.006.

ALA (2023). *Ziziphus mauritiana* Lam. In: *Atlas of Living Australia*. Canberra, Australia: Atlas of Living Australia (ALA). Available at https://bie.ala.org.au/species/https://id.biodiversity.org.au/node/apni/2894258 [modified on: Fri, 14 Apr, 2023]

Aldhanhani ARH, Ahmed ZFR, Tzortzakis N, Singh Z (2022). Maturity stage at harvest influences antioxidant phytochemicals and antibacterial activity of jujube fruit (*Ziziphus mauritiana* Lamk. and *Ziziphus spina-christi* L.). Ann Agric Sci 67(2):196-203. DOI:10.1016/j.aoas.2022.12.003.

Al-Saif AM, Abdel-Sattar M, Aboukarima AM, Eshra DH (2021). Identification of Indian jujube varieties cultivated in Saudi Arabia using an artificial neural network. Saudi J Biol Sci 28(10):5765-5772. DOI:10.1016/j.sjbs.2021.06.019.

Alsayari A, Wahab S (2021). Genus *Ziziphus* for the treatment of chronic inflammatory diseases. Saudi J Biol Sci 28(12):6897-6914. DOI:10.1016/j.sjbs.2021.07.076.

Amin W, Hussain W, Anjum MA, Ejaz S, Saqib M, Khalid M, et al. (2018). Genetic diversity of jujube (*Ziziphus mauritiana*) cultivars. Genetika 50(2):483-494. DOI:10.2298/GENSR1802483A.

Arndt SK, Wanek W, Clifford SC, Popp M (2000). Contrasting adaptations to drought stress in field-grown *Ziziphus mauritiana* and *Prunus persica* trees: Water relations, osmotic adjustment and carbon isotope composition. Aust J Plant Physiol 27(11):985-996. DOI:10.1071/PP00022.

Azam-Ali S, Bonkoungou E, Bowe C, deKock C, Godara A, Williams JT (2006). *Fruits for the Future. 2. Ber and Other Jujubes, revised edition.* Southampton, UK: Centre for Underutilised Crops. Available at: https://web.archive.org/web/20121005002217/http://www.cropsforthefuture.org/publication/Monographs/Ber%20and%20other%20Jujubes%20monograph.pdf.

Bal JS (1992). Identification of ber (*Zizyphus mauritiana* Lamk.) cultivars through vegetative and fruit characters. In: Blazek J, editors. *Fruit Breeding and Genetics*. (Acta Horticulturae, No. 317). Korbeek-Lo, Belgium: International Society for Horticultural Science (ISHS), pp. 245-253. Available at: https://www.actahort.org/books/317/317_30.htm.

Chiou C-Y, Shih H-C, Tsai C-C, Jin X-L, Ko Y-Z, Mantiquilla J-A, et al. (2020). The genetic relationships of Indian jujube (*Ziziphus mauritiana* Lam.) cultivars using SSR markers. Heliyon 6(10):e05078 [11pp]. DOI:10.1016/j.heliyon.2020.e05078.

Choi S-H, Ahn J-B, Kozukue N, Levin CE, Friedman M (2011). Distribution of free amino acids, flavonoids, total phenolics, and antioxidative activities of Jujube (*Ziziphus jujuba*) fruits and seeds harvested from plants grown in Korea. J Agric Food Chem 59(12):6594-6604. DOI:10.1021/jf200371r.

Choi S-H, Ahn J-B, Kim H-J, Im N-K, Kozukue N, Levin CE, et al. (2012). Changes in free amino acid, protein, and flavonoid content in jujube (*Ziziphus* jujube) fruit during eight stages of growth and antioxidative and cancer cell inhibitory effects by extracts. J Agric Food Chem 60(41):10245-10255. DOI:10.1021/jf302848u.

Dairou S, Biyanzi P, Pallet D, Ndjouenkeu R (2014). Traditional production, processing and quality attributes of *Ziziphus mauritiana* in Savannah region of Cameroon. J Sci Res Rep 3(5):686-699. DOI:10.9734/JSRR/2014/5638.

Dalal N, Neeraj, Bisht V (2019). Value added products from Ber. Int J Curr Microbiol Appl Sci 8(1):1603-1615. DOI:10.20546/ijcmas.2019.801.169.

Delfanian M, Esmaeilzadeh Kenari R, Sahari MA (2016). Utilization of jujube fruit (*Ziziphus mauritiana* Lam.) extracts as natural antioxidants in stability of frying oil. Int J Food Prop 19(4):789-801. DOI:10.1080/10942912.2015.1043638.

Dureja AG, Dhiman K (2012). Free radical scavenging potential and total phenolic and flavonoid content of *Ziziphus mauritiana* and *Ziziphus nummularia* fruit extracts. Int J Green Pharmacy 6(3):187-192. DOI:10.4103/0973-8258.104929.

FAO (2001). *Under-Utilized Tropical Fruits of Thailand*. (RAP Publication: 2001/26). Bangkok, Thailand: Food and Agriculture Organization of the United Nations (FAO), Regional Office for Asia and the Pacific. Available at: https://www.fao.org/publications/card/en/c/96e3d4b4-8ee0-549a-8ad2-ef8e645bc95f/.

Hasan SMK, Kabir MR, Kabir MR, Islam MR, Akhter MJ, Moury JY (2022). Proximate composition, minerals, phytochemicals, and functional activities of jujube fruits grown in Bangladesh. J Agric Food Res 8:100302 [7pp]. DOI:10.1016/j.jafr.2022.100302.

Jarald EE, Joshi SB, Jain DC (2009). Antidiabetic activity of extracts and fraction of Zizyphus mauritiana. Pharm Biol 47(4):328-334. DOI:10.1080/13880200902752488.

Jin X (2018). Jujuba—*Ziziphus jujuba*. In: Rodrigues S, de Oliveira Silva E, Sousa de Brito E, editors. *Exotic Fruits Reference Guide*. London, UK / San Diego (CA): Academic Press, an imprint of Elsevier, pp. 263-269. Available at: https://www.sciencedirect.com/science/article/pii/B9780128031384000344.

Kaur R, Kaur U, Walia H (2015). Evaluation of free radical scavenging activities of aqueous extracts of fruits of *Ziziphus mauritiana* and *Eriobotrya japonica* through *in vitro* antioxidant assays. Glob J Res Rev 2(1):30-36.

Kavitha C, Kuna A, Sagar SB, Supraja T, Padmavathi TVN, Prabhakar BN (2014). Evaluation of physicochemical and antioxidant properties of ber (Zizyphus mauritiana Lam.) and RTS ber beverage. Biochem Cell Arch 14(1):217-222.

Koley TK, Kaur C, Nagal S, Walia S, Jaggi S, Sarika (2016). Antioxidant activity and phenolic content in genotypes of Indian jujube (*Zizyphus mauritiana* Lamk.). Arab J Chem 9(Suppl. 2):S1044-S1052. DOI:10.1016/j.arabjc.2011.11.005.

Krishna H, Parashar A (2013). Phytochemical constituents and antioxidant activities of some Indian jujube (*Ziziphus mauritiana* Lamk.) cultivars. J Food Biochem 37(5):571-577. DOI:10.1111/jfbc.12008.

Kushwaha P, Yadav S, Singh V, Dwivedi L (2019). GC-MS analysis of bio-active compounds in methanolic extract of *Ziziphus mauritiana* fruit. Int J Pharm Sci Res 10(6):2911-2916. DOI:10.13040/IJPSR.0975-8232.10(6).2911-16.

Lim TK (2012). *Ziziphus mauritiana*. In: *Edible Medicinal and Non-Medicinal Plants: Volume 5, Fruits*. Dordrecht, Germany: Springer Science+Business Media, pp. 605-613. Available at: https://link.springer.com/chapter/10.1007/978-94-007-5653-3_31.

Maruza IM, Musemwa L, Mapurazi S, Matsika P, Munyati VT, Ndhleve S (2017). Future prospects of *Ziziphus mauritiana* in alleviating household food insecurity and illnesses in arid and semi-arid areas: A review. World Dev Perspect 5:1-6. DOI:10.1016/j.wdp.2017.01.001.

Mateen A, Phanikumar G (2018). Development, evaluation and optimization of Ber (*Ziziphus mauritiana* Lam.) based Kiwifruit jam. Int J Food Sci Nutr 3(4):99-106.

Mathangi S, Maran JP (2020). A study on Apple ber to identify the suitability of new product development. Plant Sci Today 7(1):61-69. DOI:10.14719/pst.2020.7.1.640.

Memon A, Memon N, Bhanger MI, Luthria DL (2012). Phenolic acids composition of fruit extracts of ber (*Ziziphus mauritiana* L., *var*. Golo Lemai). Pak J Anal Environ Chem 13(2):37-42.

Memon AA, Memon N, Bhanger MI, Luthria DL (2013). Assay of phenolic compounds from four species of ber (*Ziziphus mauritiana* L.) fruits: comparison of three base hydrolysis procedure for quantification of total phenolic acids. Food Chem. 139(1-4):496-502. DOI:10.1016/j.foodchem.2013.01.065.

Morton J (1987). Indian Jujube. p. 272–275. In: *Fruits of Warm Climates* [Julia F. Morton, Miami, FL]. Hosted by West Lafayette (IN): Purdue University, Horticulture and Landscape Architecture. Available at: https://www.hort.purdue.edu/newcrop/morton/indian_jujube.html.

Muhammad N, Luo Z, Yang M, Liu Z, Liu M (2022). The nutritional, medicinal, and drought-resistance properties of *Ziziphus* Mill. make it an important candidate for alleviating food insecurity in arid regions—A case of Pakistan. Horticulturae 8(10):867 [14pp]. DOI:10.3390/horticulturae8100867.

Nyanga LK (2012). *Ziziphus mauritiana (Masau) Fruits Fermentation In Zimbabwe: From Black-box to Starter Culture Development [M.D. Thesis]*. Wageningen, The Netherlands: Wageningen University, Available at: https://edepot.wur.nl/239532.

Nyanga LK, Nout MJR, Gadaga TH, Boekhout T, Zwietering MH (2008). Traditional processing of masau fruits (*Ziziphus mauritiana*) in Zimbabwe. Ecol Food Nutr 47(1):95-107. DOI:10.1080/03670240701702321.

Nyanga LK, Gadaga TH, Nout MJ, Smid EJ, Boekhout T, Zwietering MH (2013). Nutritive value of masau (*Ziziphus mauritiana*) fruits from Zambezi Valley in Zimbabwe. Food Chem 138(1):168-172. DOI:10.1016/j.foodchem.2012.10.016.

Oshima N, Zaima K, Kamakura H, Hamato A, Yamamoto Y, Kang DH, et al. (2014). Identification of marker compounds for Japanese Pharmacopoeia non-conforming jujube seeds from Myanmar. J Nat Med 69(1):68-75. DOI:10.1007/s11418-014-0864-6.

Padmanabhan S, Vishwanatha S, Narasimhamurthy K, Rao SV (1993). Effect of feeding her (*Zizyphus mauritiana* Lam.) juice on growth, blood composition and histology of albino rats. Int J Food Sci Nutr 44(2):91-94. DOI:10.3109/09637489309017427.

Palejkar CJ, Palejkar JH, Patel AJ, Patel MA (2012). A plant review on *Ziziphus mauritiana*. Int J Univers Pharm Life Sci 2(2):202-211.

Pareek OP (2001). *Fruits for the Future: Ber*. (Factsheet No. 2, February 2001). Southampton, UK: University of Southampton, International Centre for Underutilised Crops.

Pareek S (2013). Nutritional composition of jujube fruit. Emir J Food Agric 25(6):463-470. DOI:10.9755/ejfa.v2516.15552.

Paul NR, Mallick S, Zakir HM, Rahman A, Quadir QF (2021). Nutritional and Biochemical quality assessment of commonly consumed jujube (*Zizyphus mauritiana* L.) varieties available in Bangladesh. J Exp Agric Int 43(3):30-41. DOI:10.9734/JEAI/2021/v43i330654.

Petrie CA, Bates J (2017). 'Multi-cropping', intercropping and adaptation to variable environments in Indus South Asia. J World Prehist 30(2):81-130. DOI:10.1007/s10963-017-9101-z.

Prakash O, Usmani S, Singh R, Singh N, Gupta A, Ved A (2021). A panoramic view on phytochemical, nutritional, and therapeutic attributes of *Ziziphus mauritiana* Lam.: A comprehensive review. Phytother Res 35(1):63-77 [plus supplementary figures]. DOI:10.1002/ptr.6769.

Rashwan AK, Karim N, Shishir MRI, Bao T, Lu Y, Chen W (2020). Jujube fruit: A potential nutritious fruit for the development of functional food products. J Funct Foods 75:104205 [16pp]. DOI:10.1016/j.jff.2020.104205.

Razi F-u-DM, Anwar R, Basra SMA, Mumtaz Khan M, Khan IA (2013). Morphological characterization of leaves and fruit of jujube (*Ziziphus mauritiana* Lamk.) germplasm in Faisalabad, Pakistan. Pak J Agric Sci 50(2):211-216.

Safizadeh B, Hoshyar R, Hemmati M, Zarban A, Ebrahimi R (2016). A preliminary evaluation of effects of high doses of Jujube and Saffron on biochemical and hematological parameters in rats. Clin Phytosci 2(1):15 [5pp]. DOI:10.1186/s40816-016-0029-0.

Shahrajabian MH, Khoshkharam M, Zandi P, Sun W, Cheng Q (2019). Jujube, a super-fruit in traditional Chinese medicine, heading for modern pharmacological science. J Med Plants Stud 7(4):173-178.

Shams ZA, Wadhawan N (2019). Development and shelf life assessment of a carbonated RTS beverage from ber fruit (*Ziziphus mauritiana*). Int J Sci Environ Technol 8(1):193-200.

Sharif M, Naz A, Farooq U, Razzaq K, Sher MA, Khan M, et al. (2022). A comprehensive investigation of novel Ber (*Ziziphus mauritiana*) products from South Punjab, Pakistan. J Bioresour Manag 9(2):15-31.

Siriamornpun S, Weerapreeyakul N, Barusrux S (2015). Bioactive compounds and health implications are better for green jujube fruit than for ripe fruit. J Funct Foods 12:246-255. DOI:10.1016/j.jff.2014.11.016.

Suryanarayan A, Cubas M, Craig OE, Heron CP, Shinde VS, Singh RN, et al. (2021). Lipid residues in pottery from the Indus Civilisation in northwest India. J Archaeol Sci 125:105291 [16pp]. DOI:10.1016/j.jas.2020.105291.

TFDA (2017). Indian dates, Indian Jujube. In: *[Consolidated List of Raw Materials Available for Food]*. Taipei City, Taiwan, People's Republic of China: Taiwan Food and Drug Administration (TFDA), Ministry of Health and Welfare. Available at: https://consumer.fda.gov.tw/Food/MaterialDetail.aspx?nodeID=160&id=17211 [© 2017].

U.S. FDA (2016). *Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues*. (Docket Number: FDA-2011-D-0376). College Park (MD): U.S. Food and Drug Administration (U.S. FDA), Center for Food Safety and Applied Nutrition (CFSAN). Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/draft-guidance-industry-new-dietary-ingredient-notifications-and-related-issues [August 2016].

U.S. FDA (2018). *Guidance for Industry: Reference Amounts Customarily Consumed (List of Products for Each Product Category)*. (Docket Number: FDA-2016-D-4098). Silver Spring (MD): U.S. Food and Drug Administration (U.S. FDA), Center for Food Safety and Applied Nutrition (CFSAN). Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-reference-amounts-customarily-consumed-list-products-each-product-category [March 2018].

U.S. FDA (2022a). Part 184—Direct food substances affirmed as generally recognized as safe. Section §184.1444—Maltodextrin. In: *U.S. Code of Federal Regulations (CFR). Title 21: Food and Drugs*. (U.S. Food and Drug Administration). Washington (DC): U.S. Government Printing Office (GPO). Available at: https://www.govinfo.gov/app/collection/cfr/2022/title21.

U.S. FDA (2022b). Part 20—Public information. §20.61—Trade secrets and commercial or financial information which is privileged or confidential. In: *U.S. Code of Federal Regulations (CFR). Title 21: Food and Drugs*. (U.S. Food and Drug Administration). Washington (DC): U.S. Government Printing Office (GPO). Available at: https://www.govinfo.gov/app/collection/cfr/2022/title21.

U.S. FDA (2022c). Part 190—Dietary supplements. §190.6—Requirement for premarket notification. In: *U.S. Code of Federal Regulations (CFR). Title 21: Food and Drugs*. (U.S. Food and Drug Administration). Washington (DC): U.S. Government Printing Office (GPO). Available at: https://www.govinfo.gov/app/collection/cfr/2022/title21.

U.S. FDA (2023). Federal Food, Drug, and Cosmetic Act (FD&C Act [or, FFDCA, FDCA]): Chapter 9. Subchapter II - Definitions. 21 USC §321 - Definitions, generally [Sec. 201]. In: *U.S. Code-Title 21-Food and Drug* (Food and Drug Administration). Washington (DC): U.S. House of Representatives, Office of Law Revision Counsel. Available at: http://uscode.house.gov/browse/prelim@title21/chapter9&edition=prelim [current through Public Law 117-362 – 01/05/2023].

USDA (2019a). 'Jujube, raw'. In: *FoodData Central*. (FDC ID: 168151; NDB Number:9146). Beltsville (MD): U.S. Department of Agriculture (USDA), Agricultural Research Service (ARS). Available at: https://fdc.nal.usda.gov/fdc-app.html#/food-details/168151/nutrientshttps://fdc.nal.usda.gov/fdc-app.html - /food-details/1102702/nutrients [FDC published: 4/1/2019].

USDA (2019b). 'Jujube, Chinese, fresh, dried'. In: FoodData Central. (FDC ID: 168152; NDB Number:9147). Beltsville (MD): U.S. Department of Agriculture (USDA), Agricultural Research Service (ARS). Available at: https://fdc.nal.usda.gov/fdc-app.html#/food-details/168152/nutrientshttps://fdc.nal.usda.gov/fdc-app.html - /food-details/1102702/nutrients [FDC published: 4/1/2019].

Williams TO (1998). Multiple Uses of Common Pool Resources in Semi-arid West Africa: A survey of Existing Practices and Options for Sustainable Resource Management. (Natural Resource Perspectives, No. 38, November 1998). London, UK: Overseas Development Institute (ODI). Available at: https://cdn.odi.org/media/documents/2885.pdf.

Zozio S, Servent A, Hiol A, Mbéguié-A-Mbéguié D, Cosmidis L, Lucien J-M, et al. (2015). Processed Z. mauritiana Lamk in the formula of high nutritional value cake. J Food Process Technol 6:5 [6pp]. DOI:10.4172/2157-7110.1000444.