NEW DIETARY INGREDIENT (NDI) SAFETY INFORMATION

Caesalpinia spinosa

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1. New Dietary Ingredient Identity Information

1.1 Description of the identity of the NDI

This submission provides information about a new herbal dietary ingredient recognized by its Latin binomial name, Caesalpinia spinosa. Additionally, it goes by various common names, including Caesalpinia Divi-divi, tara, algarroba, huarango, guaranga, tanino, taya, and caranca. The authorship of this botanical ingredient is attributed to (Molina) Kuntze, and it is sourced from the pods and fruits of the plant.

The genus Caesalpinia L. sensu lato, belongs to the family Caesalpiniaceae (=Fabaceae, subfam. Caesalpinioideae), of pantropical distribution in forests, savannas, and semi-deserts, and includes about 150 species, of which 40 are present in South America. Two subgenera are accepted today: subg. Caesalpinia L. with species in America, Africa and Asia, characterized by a non-winged fruit, and subg. Mezoneuron (Desf.) Vidal ex Herendeen & Zarucchi, with species exclusively distributed in the Old World and with winged fruits. Species of the genus Caesalpinia are perennial trees, shrubs or herbs, some of them climbers, with pari- or imparipinnate, uni- or bipinnatic compound leaves, they may be spiny or inert. The flower has imbricate caedric sepals. The ovary consists of one carpel and develops after pollination, producing a papyrose to woody legume, which may be smooth, spiny, glandular, or covered with branched hairs.

Morphology

Caesalpinia spinosa (Molina) Kuntze is an evergreen shrub or tree, with thorns on stem and branches, 3-5(-8) m tall, and is known by a wide variety of vernacular names: tara, algarroba, huarango, guaranga, tanino, taya and caranca. The round, thorny and sometimes twisted trunk of C. spinosa has a gray bark and branches widely in foliose and thorny axes. In several cases the axes branch from near the base of the trunk, producing the impression of several trunks. The leaves are dark green, smooth, or laxly spiny and up to 10 cm long; they are bipinnatic compound paripinnate, with 2-3(-5) pairs of leaflets, which have 5-8 pairs of opposite, elliptic to ovate leaflets, 1.4-4(-4.5) cm long and 1-2.5 cm wide. The leaflets have reticulated veins, with the underside pubescent or not, and the apex obtuse to emarginate. The flowers are arranged in multiflorous terminal racemes, finely pubescent and somewhat spiny, 15(-20) cm long. The flowers, 9-10(-15) mm long, have a 5 mm long, finely pubescent peduncle. The calyx is pentamerous, asymmetrical, with sepals fused at the base, up to 6 mm long, with the ventral sepal larger, canoe-shaped and with conspicuous teeth at the apex.

The petals are yellowish-red, which at 8-9 mm long, are less than twice the length of the calyx and almost as long as the 10 stamens which are yellow. Only rarely do the stamens surpass the corolla. The fruit is light reddish-brown, flat, and often finely pubescent; it is

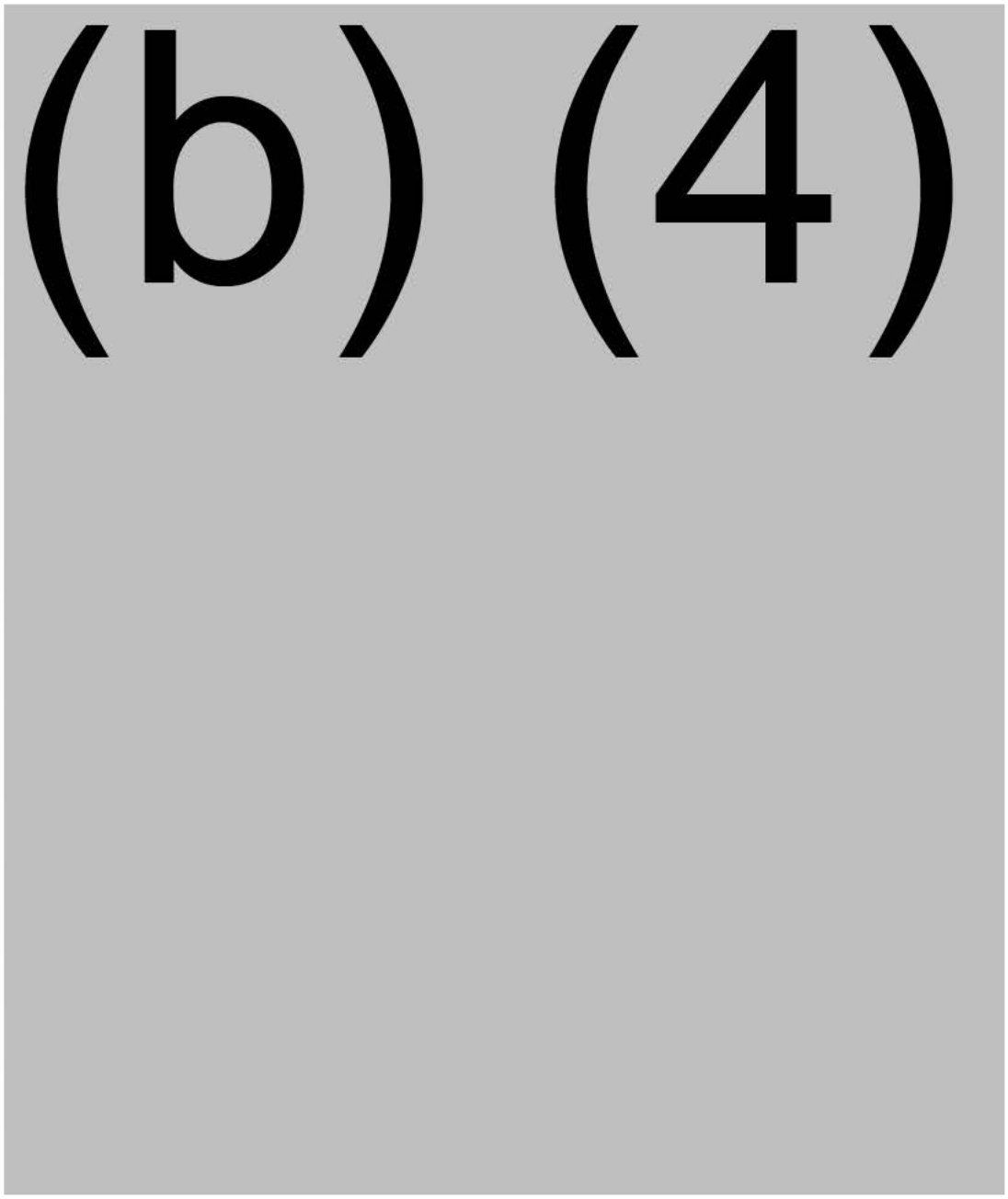
an indehiscent, leathery legume, 6-10 cm long and (1-)1.5-2.5 cm wide; at maturity it has (4-)5-8 round, black seeds. Figure 1 shows photographs of the fruit and pods of Caesalpinia spinosa.

Figure 1. Photographs of Caesalpinia spinosa. Photographs of illustration of A. Seed B. Pods C. Seeds and pods of Caesalpinia spinosa.

Caesalpinia spinosa, a shrubby legume, is primarily found in the northern regions of South America, specifically in Peru, Colombia, Venezuela, Ecuador, Bolivia, and Chile. Notably, its pods are renowned for being a rich source of tannins, primarily utilized in the leather tanning industry in Peru (Dostert et al., 2009). The plant's earliest documented reports date back to the observations made by Feuilée along the coastlines of South America and western India between 1707 and 1712. During this period, it was christened "Tara," accompanied by a concise botanical description. Subsequently, in 1782, Molina renamed the plant as Poinciana spinosa, a name that persisted until 1824. In that year, Kunth and Humboldt described a specimen discovered in Cartago, Colombia, which bore the common name "Divi-Divi" and was designated as Caesalpinia tinctoria. Finally, conforming to contemporary nomenclatural standards, the plant is officially identified as Caesalpinia spinosa (Mol.) Kuntze (Sprague, 1931).

1.2 Description of the evidence verifying the identity of the NDI

Botanic certification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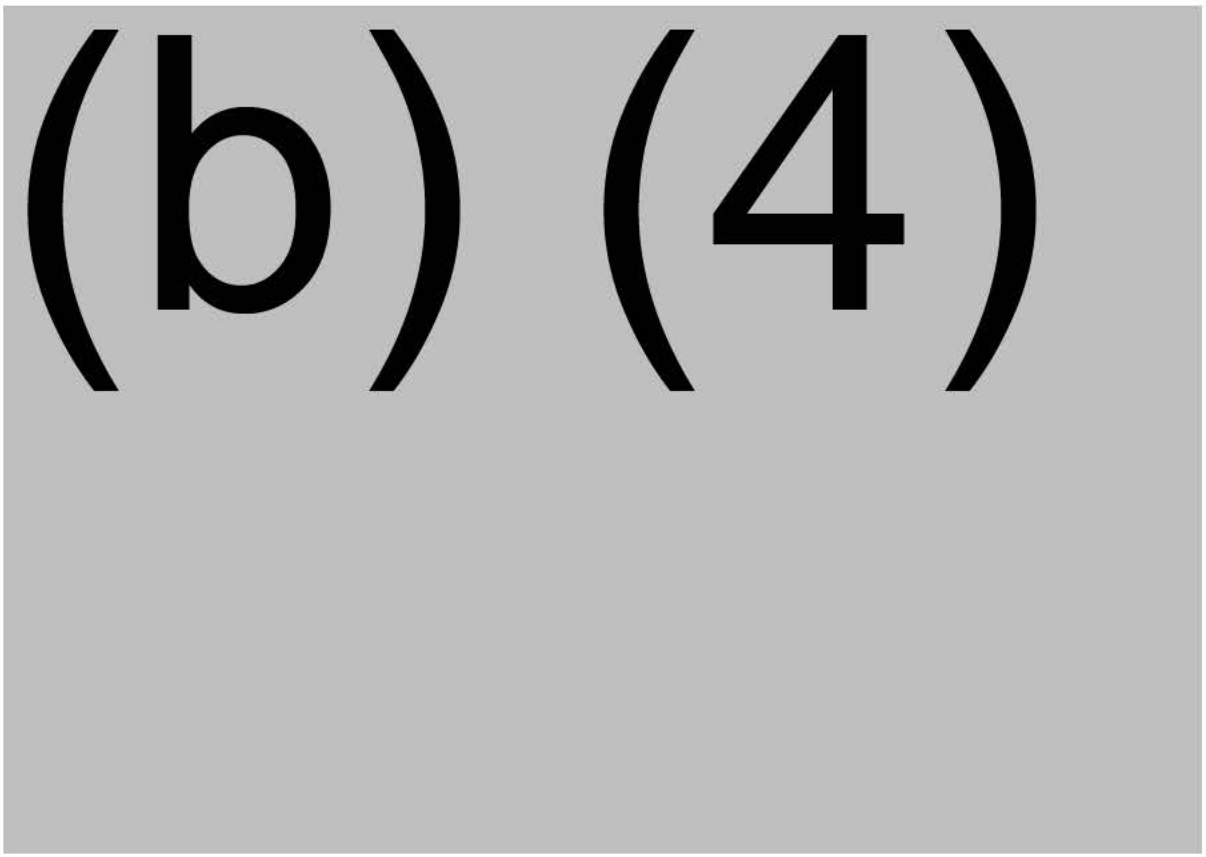
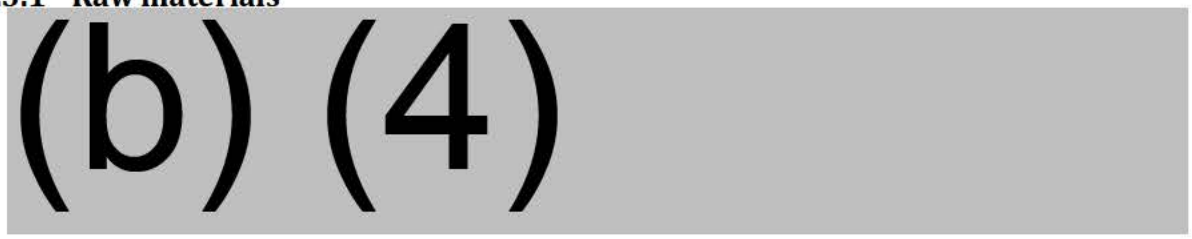
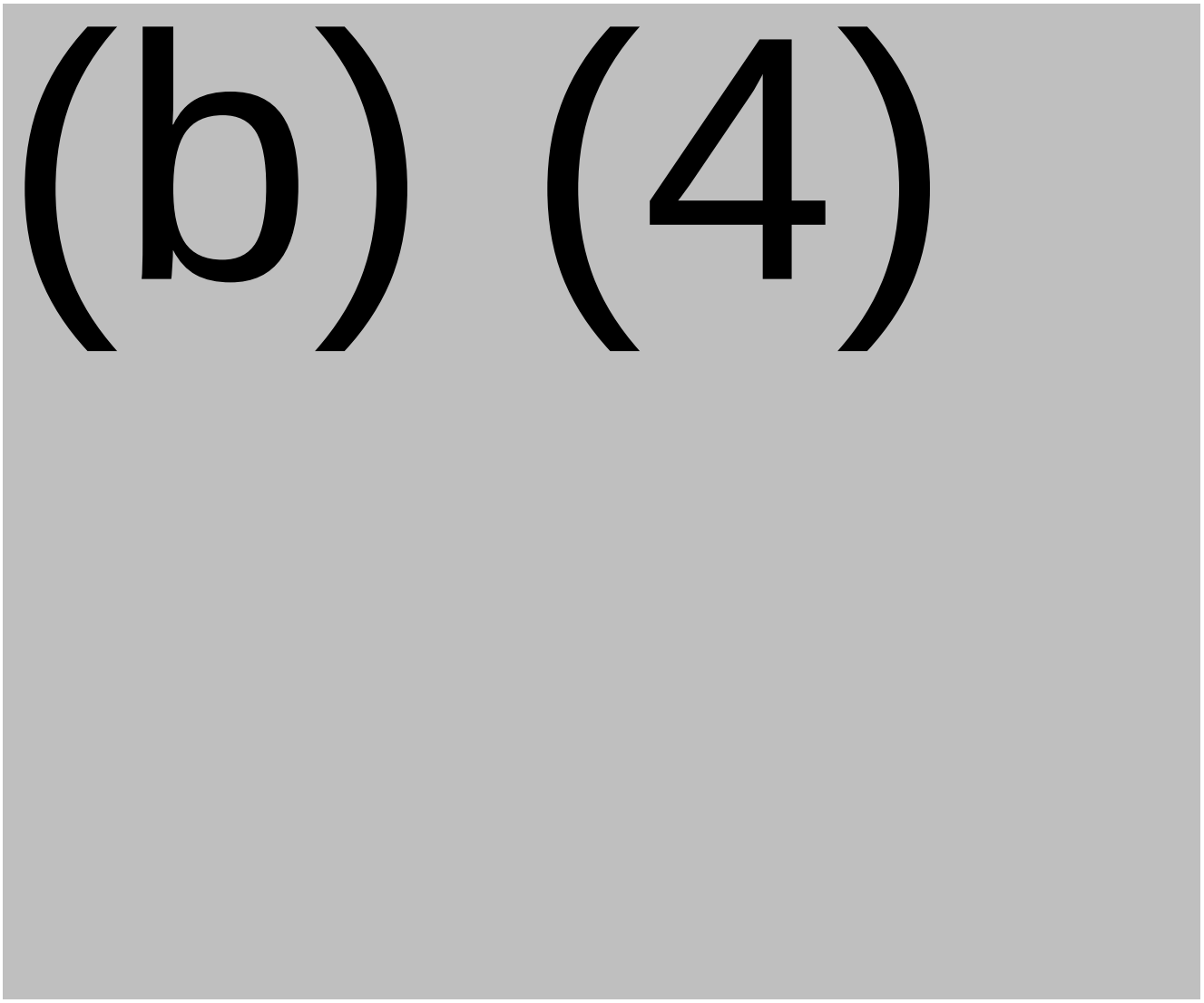


1.3 NDI manufacture

1.3.1 Raw materials

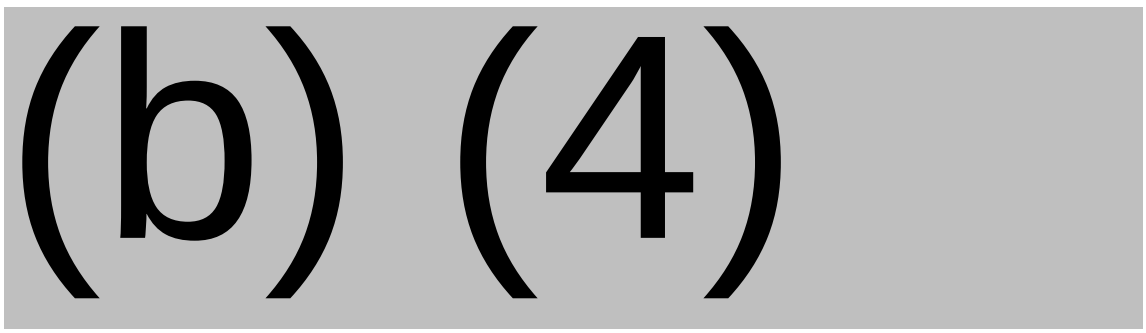


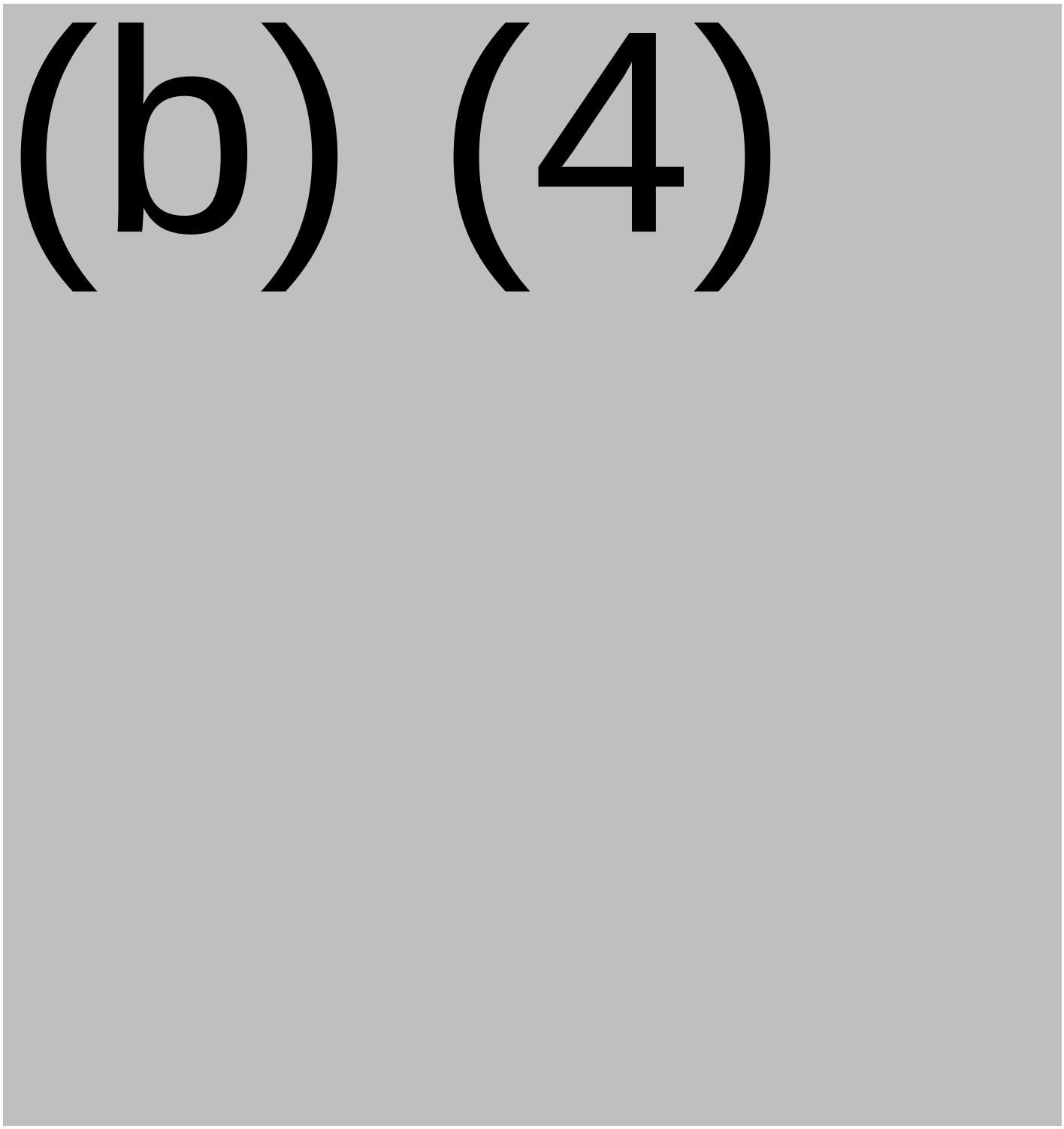


1.3.2 Formulation ingredients

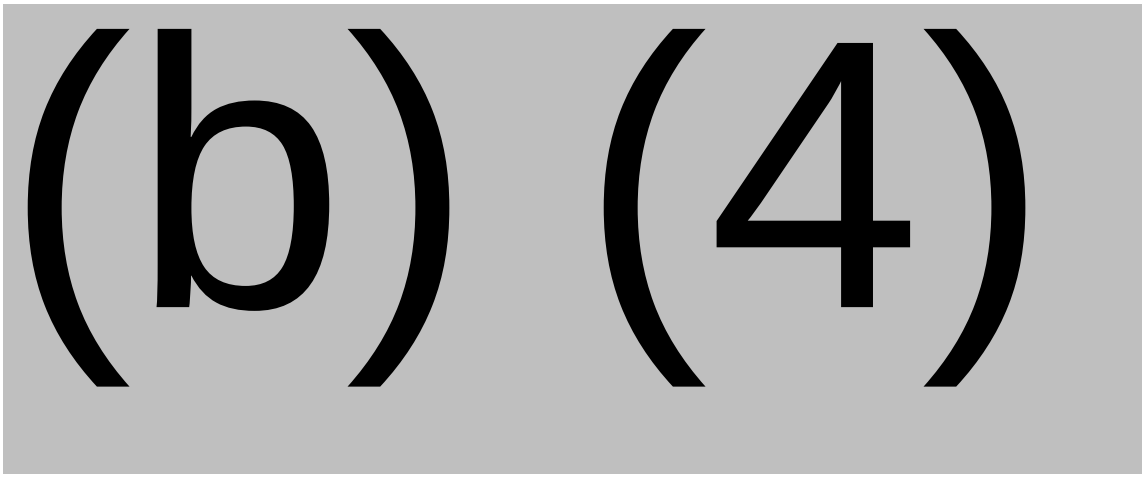
There are no formulation ingredients required other than the raw materials.

1.3.3 Manufacturing process

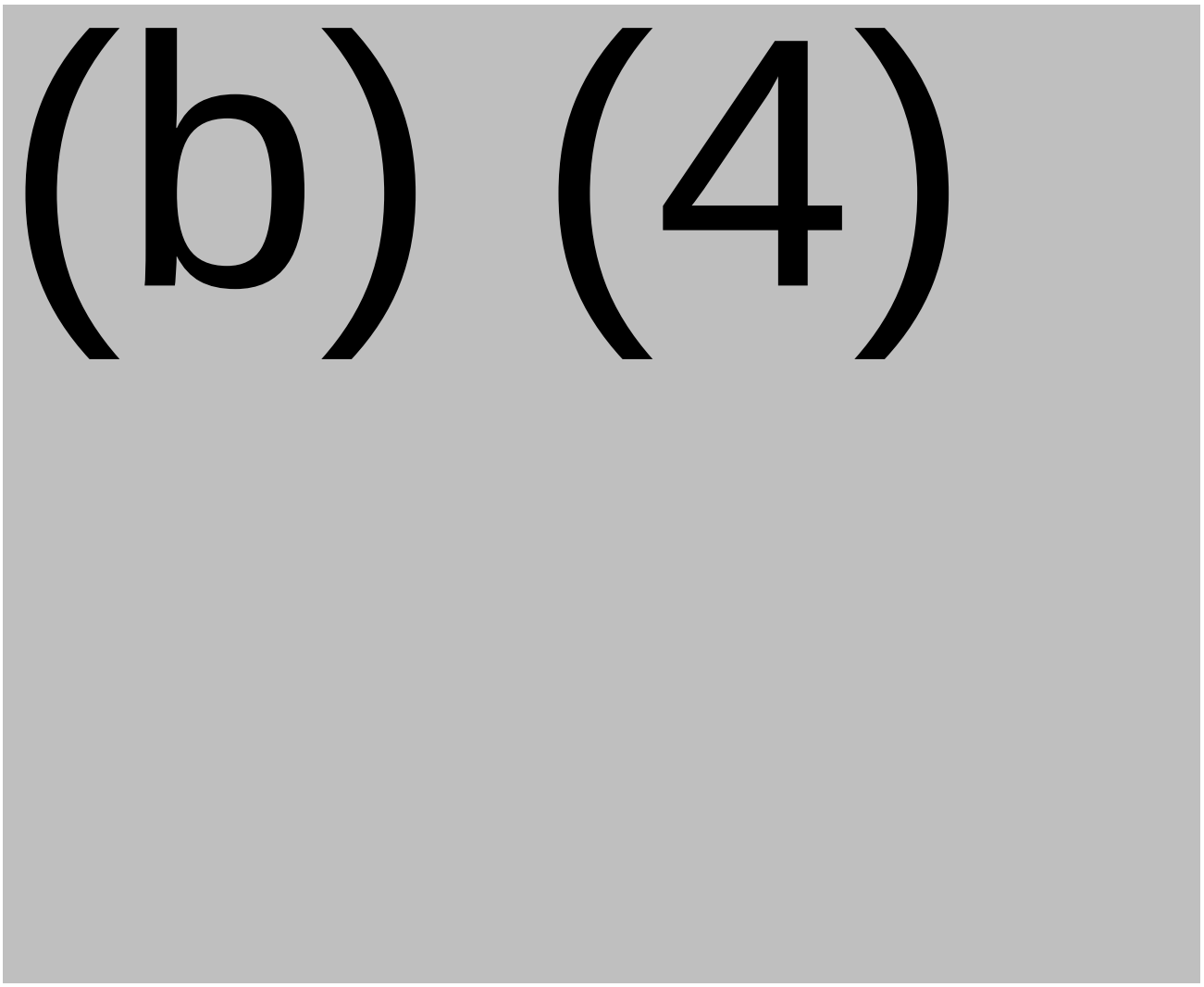


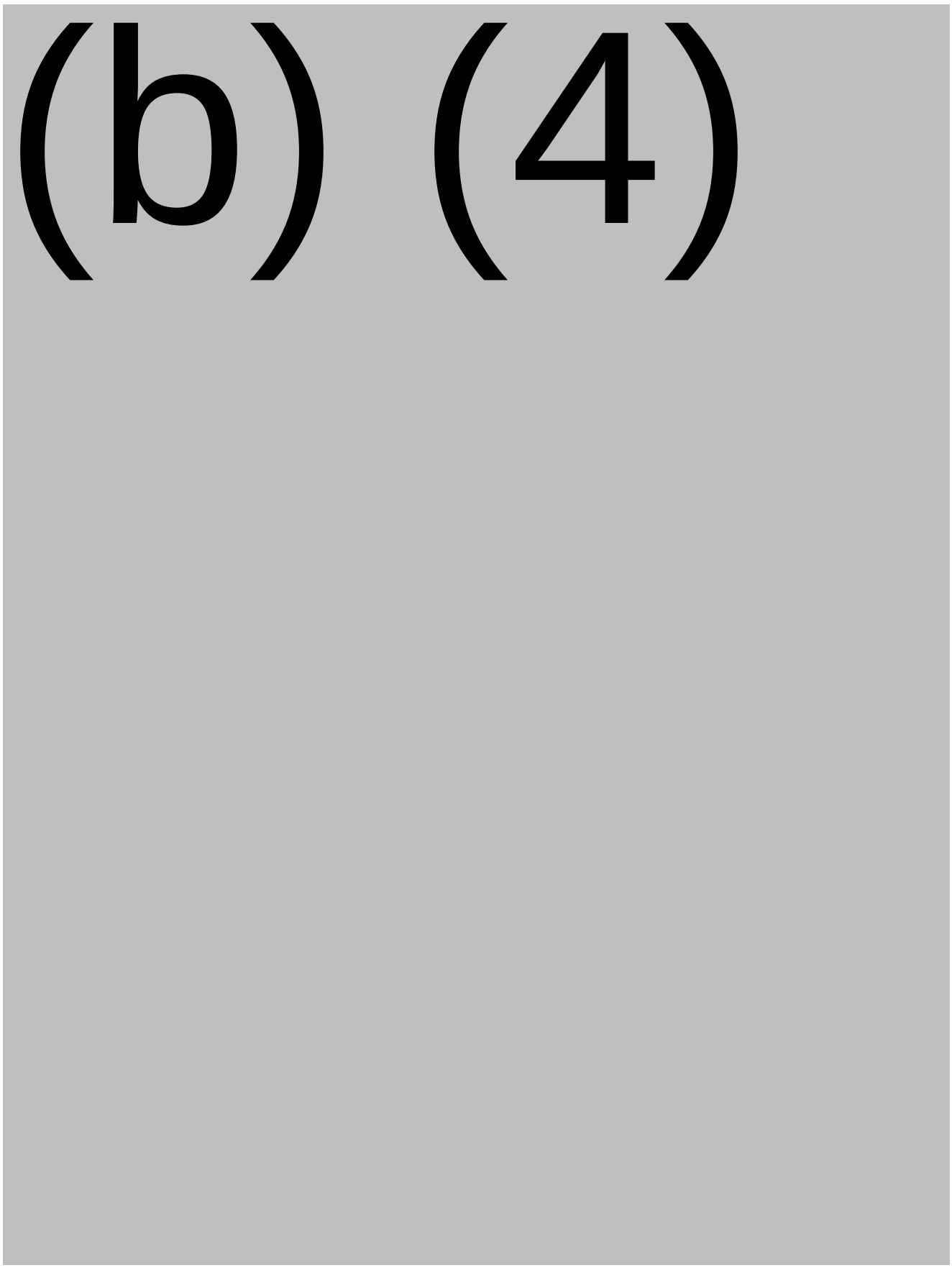


1.3.4 NDI specifications



1.3.5 Methods of analysis

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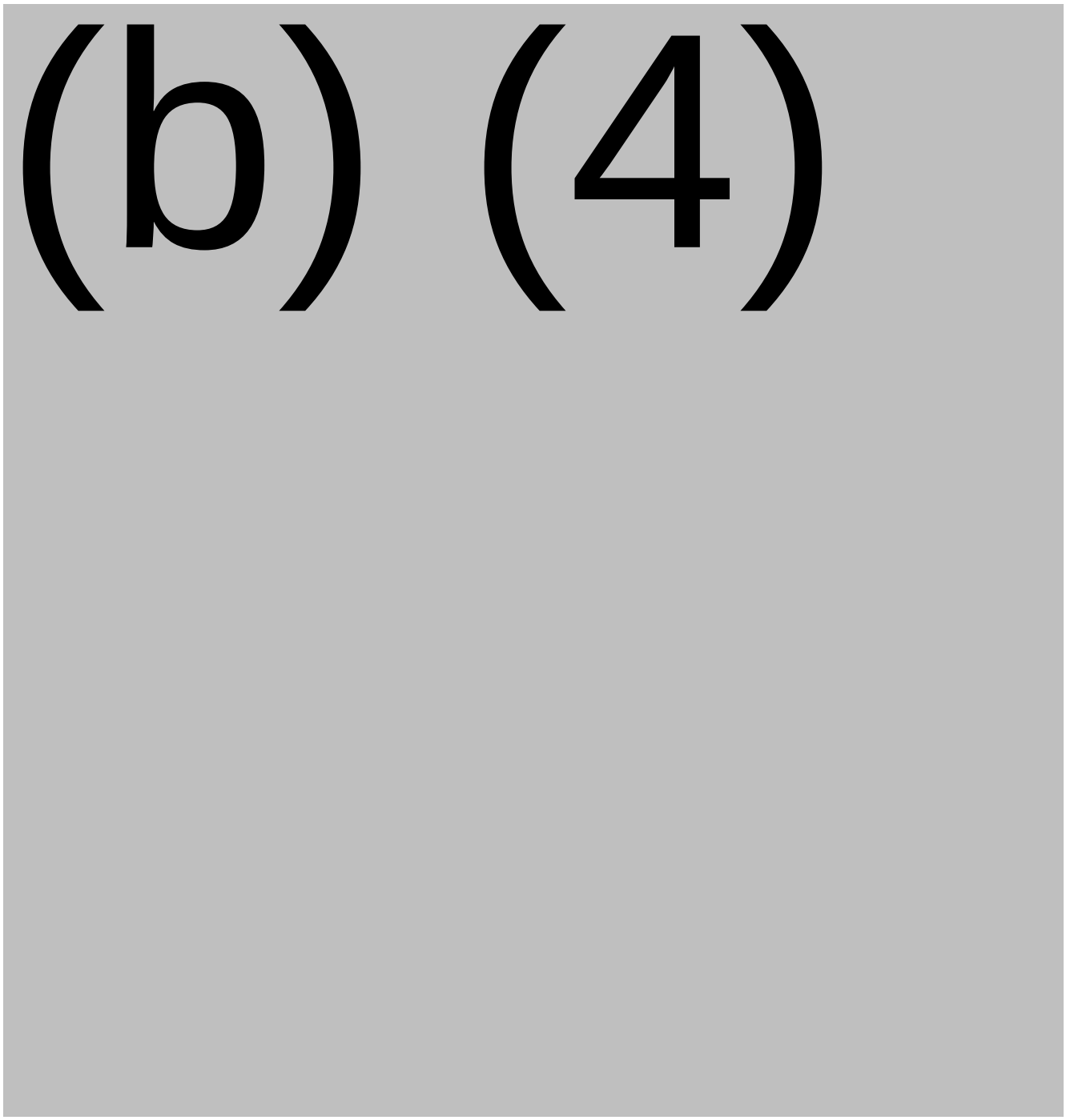
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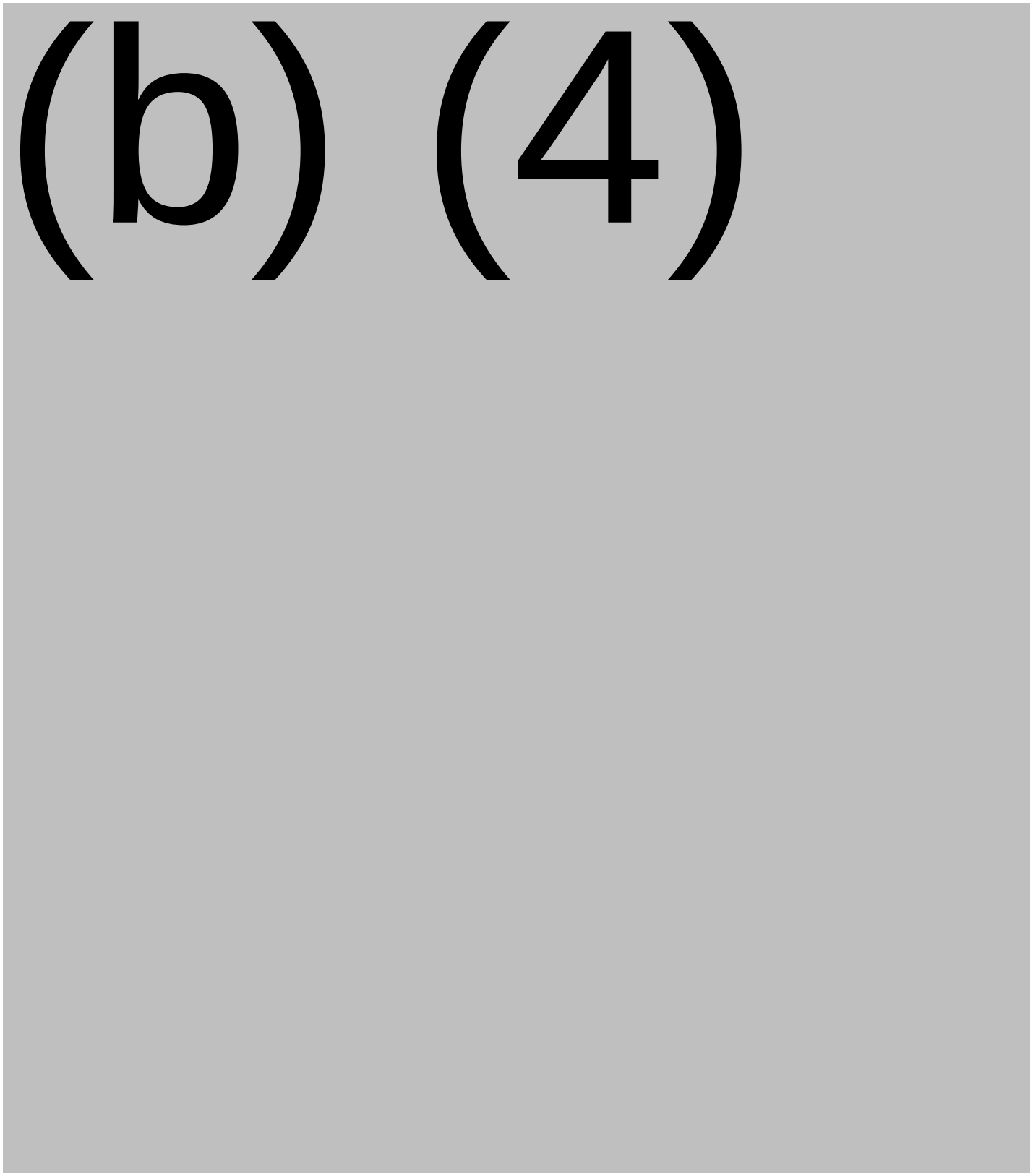
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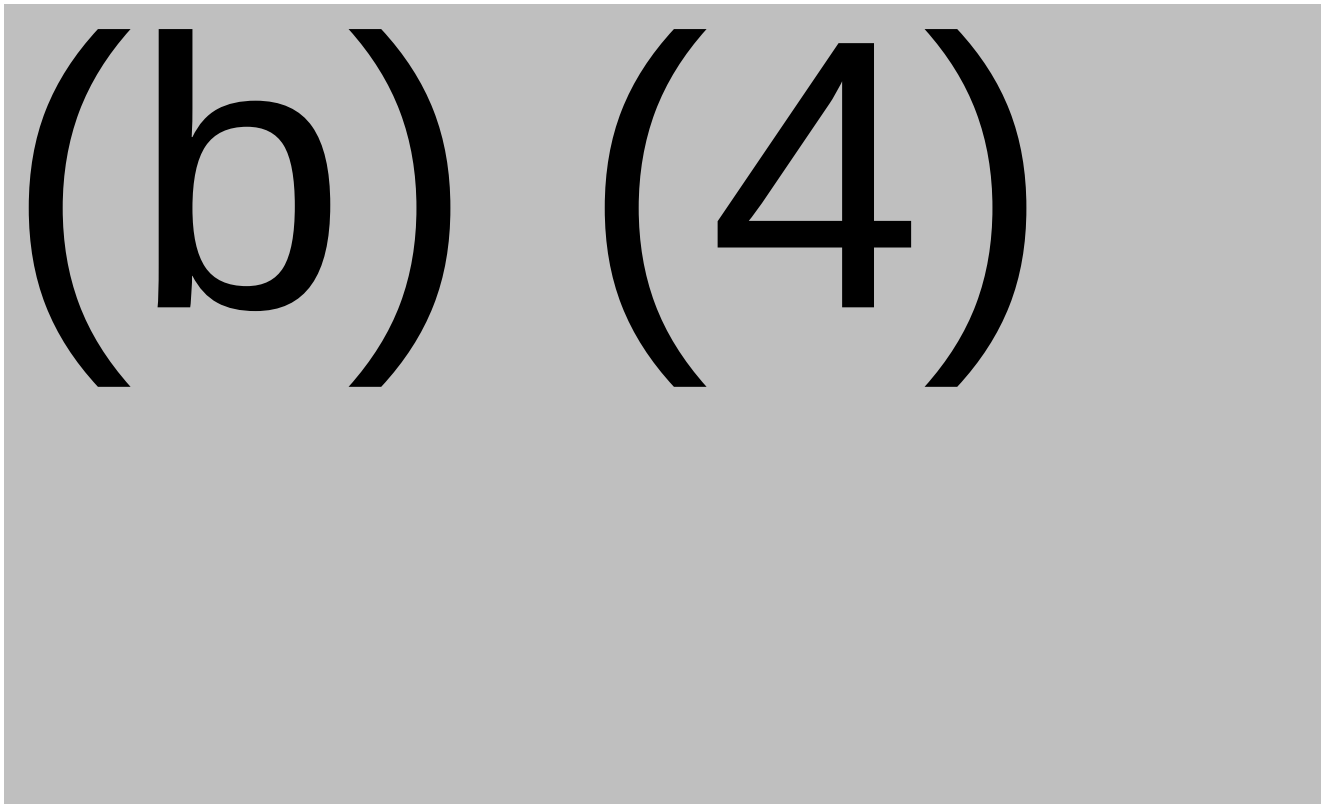
2. Dietary Supplement Manufacture

2.1. Raw material



2.2. Formulation ingredients other than the NDI

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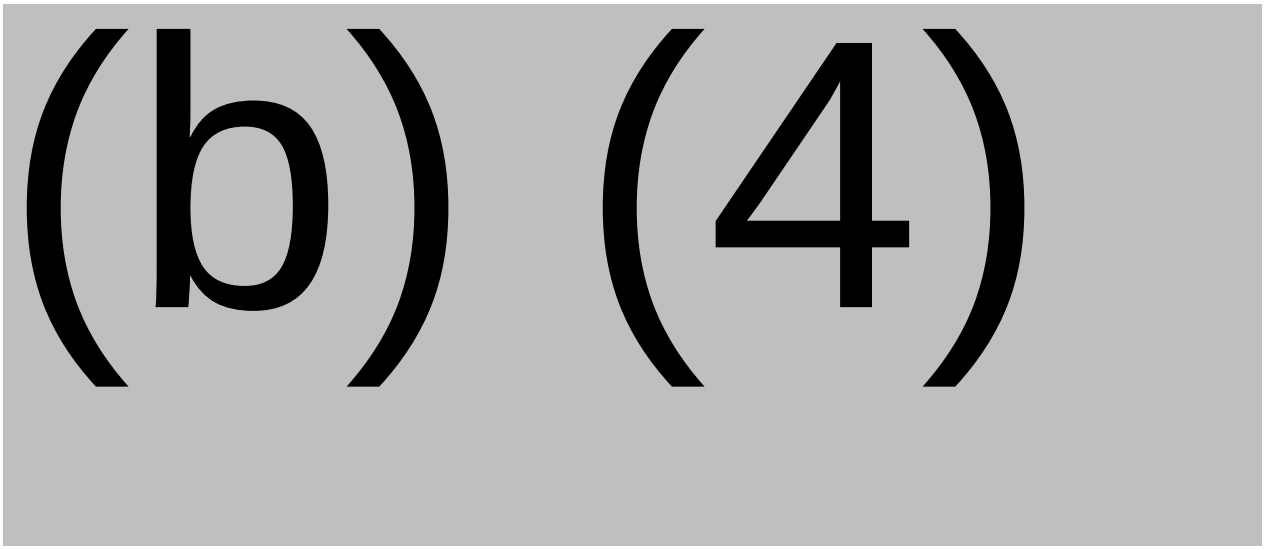
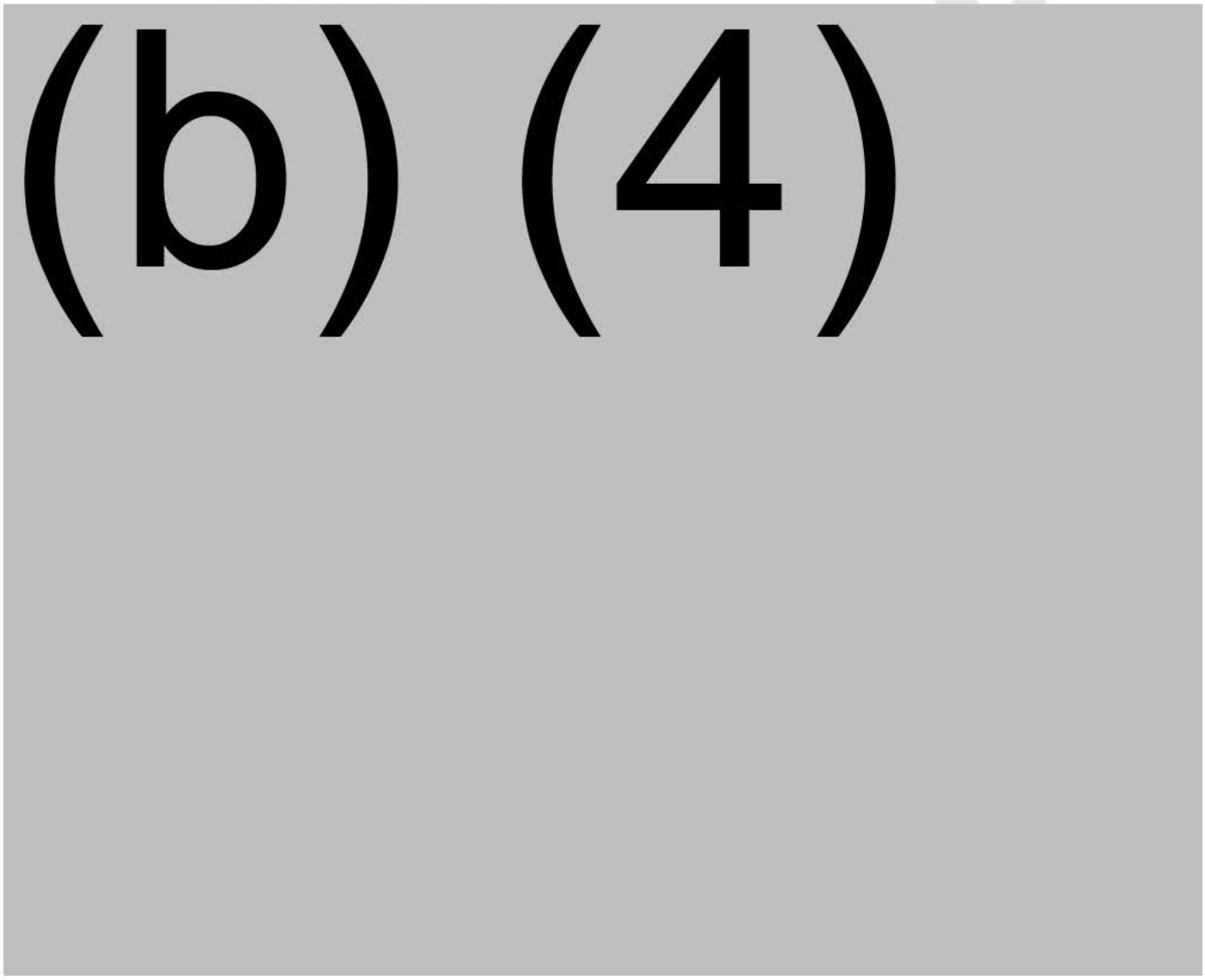
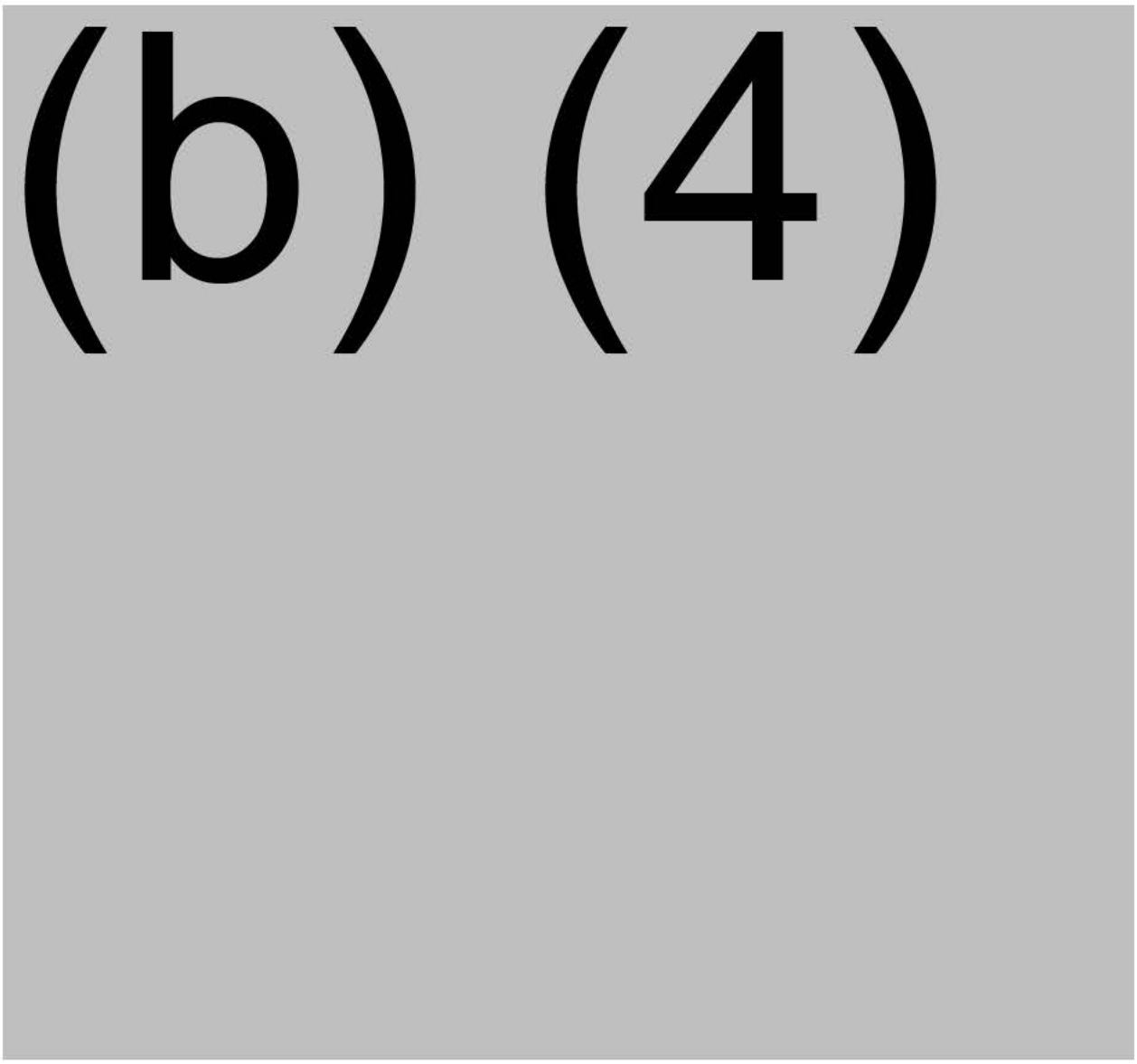
2.3. Manufacturing process



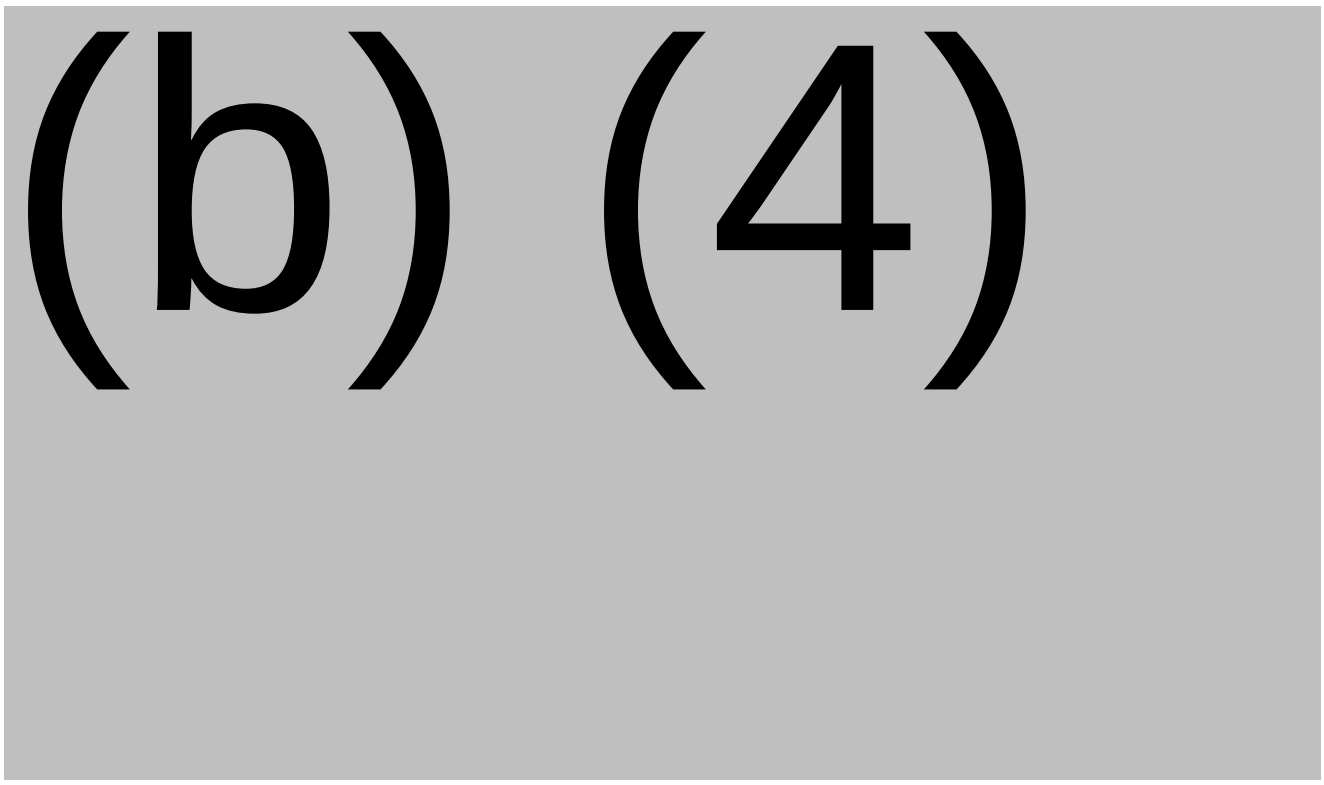
2.4. Product specifications





2.5. Methods of analysis

Materials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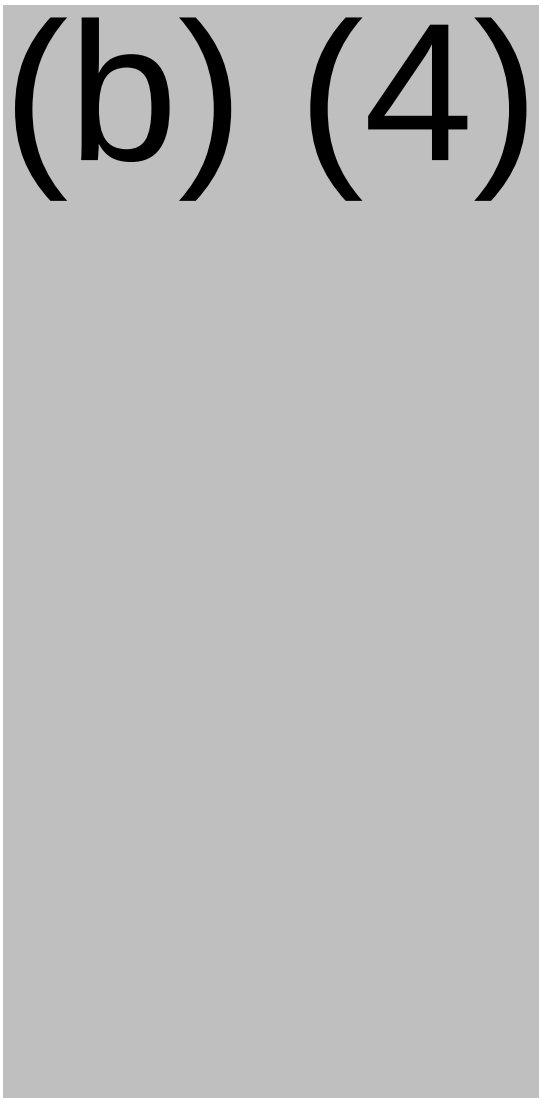
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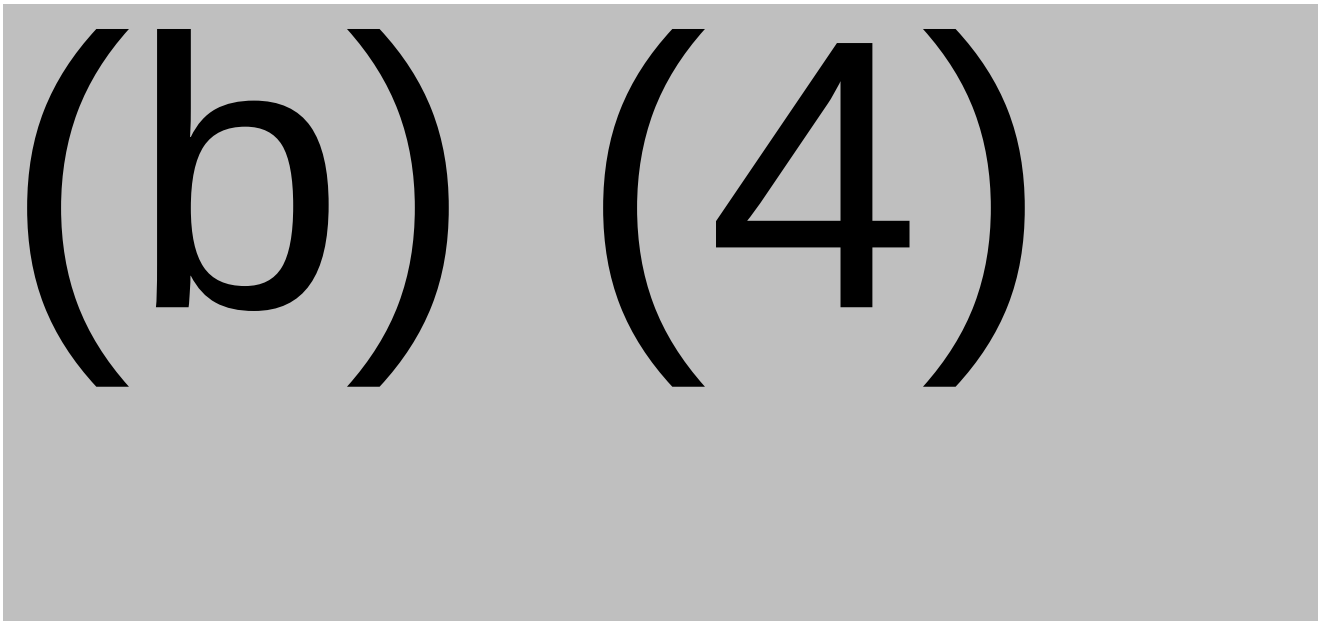
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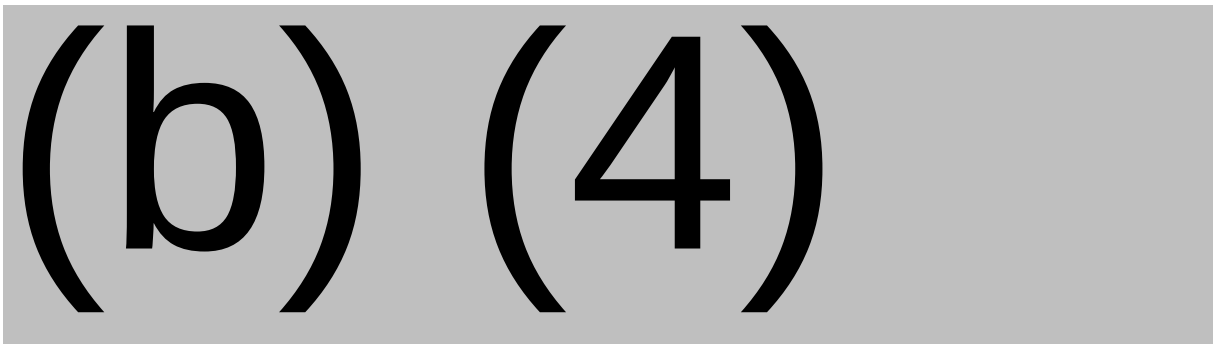
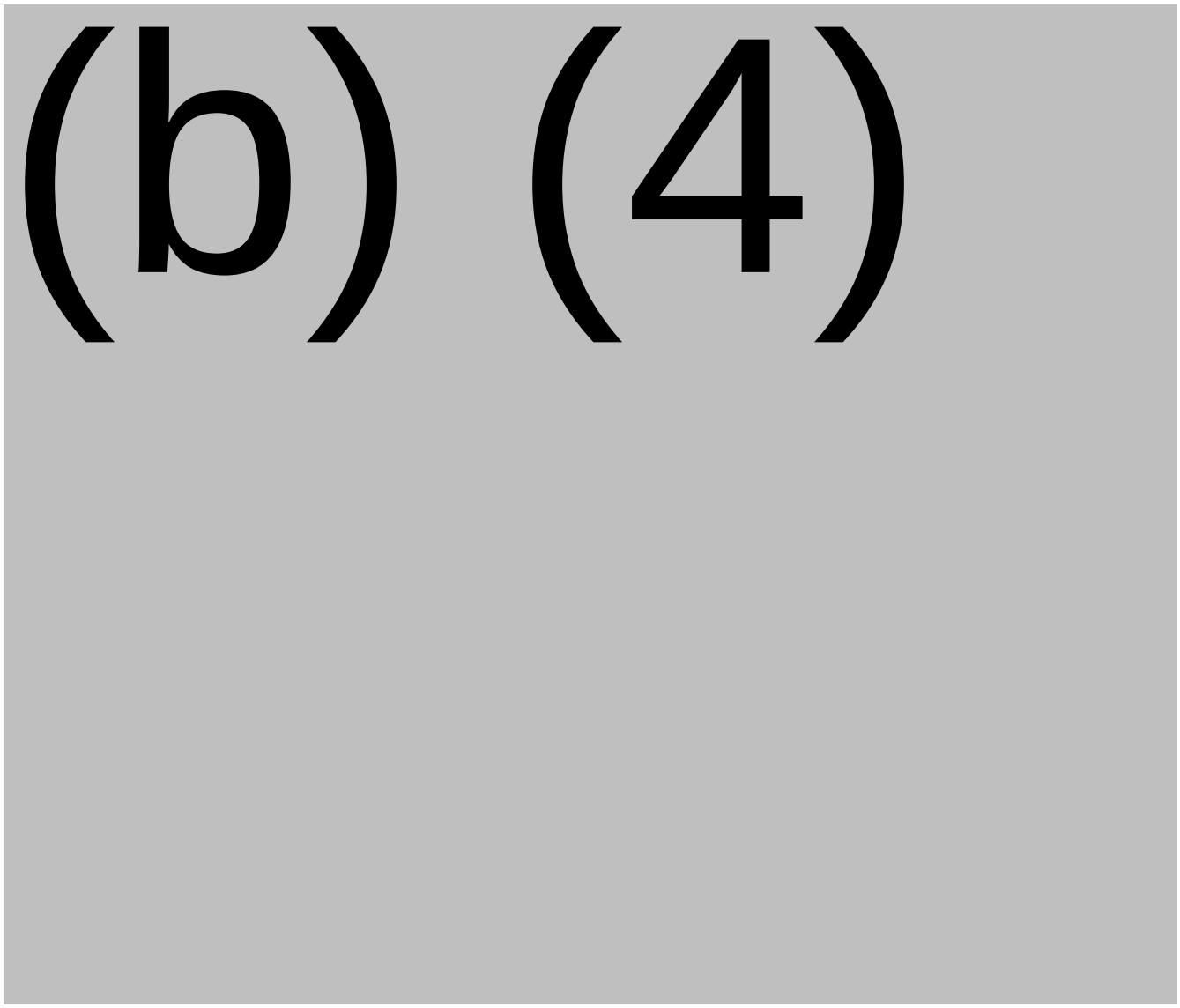
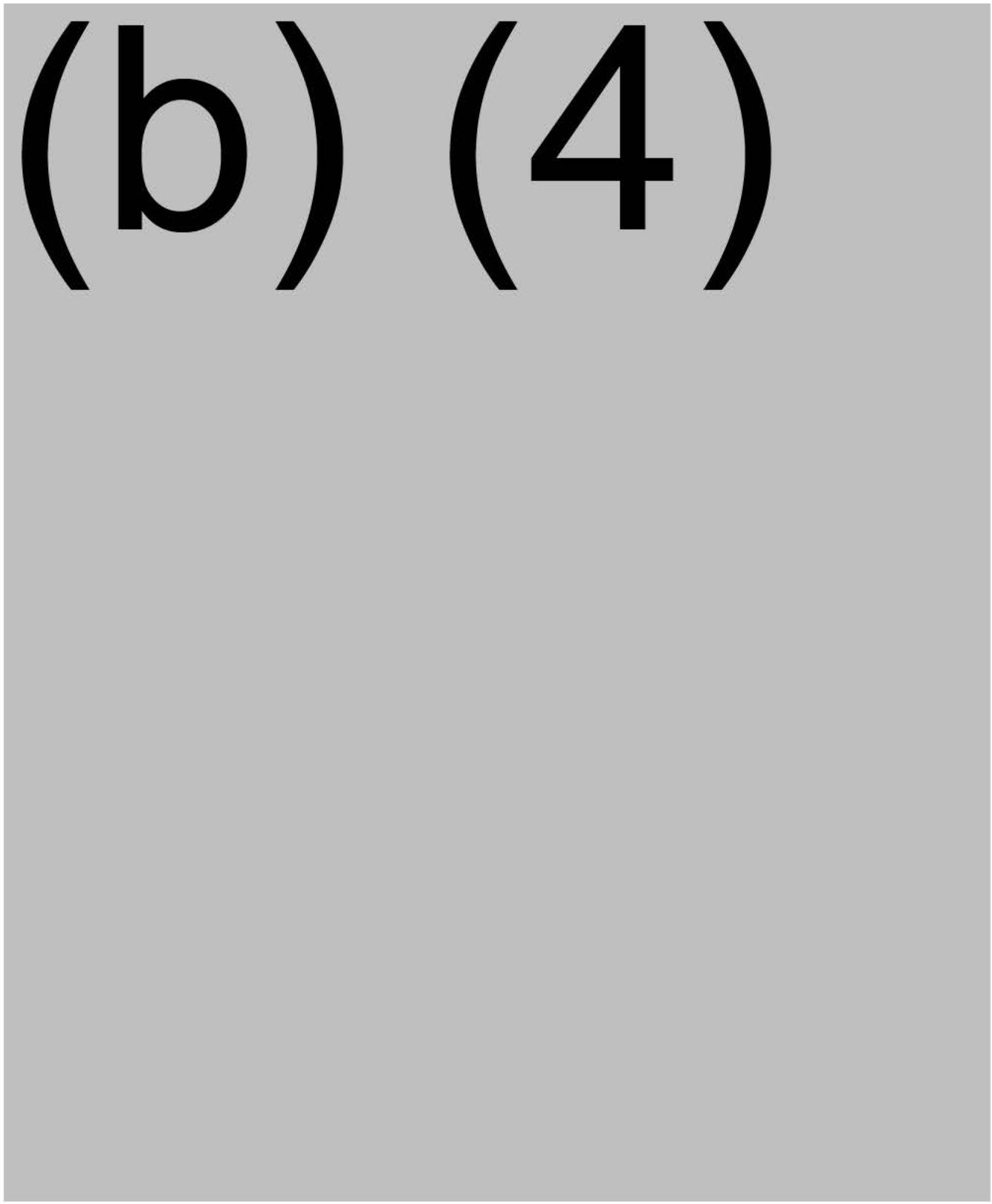


2.6. Shelf-life and conditions of storage

Based on the stability study conducted, it is recommended to store the product at room temperature below 86°F with a shelf life of 24 months.

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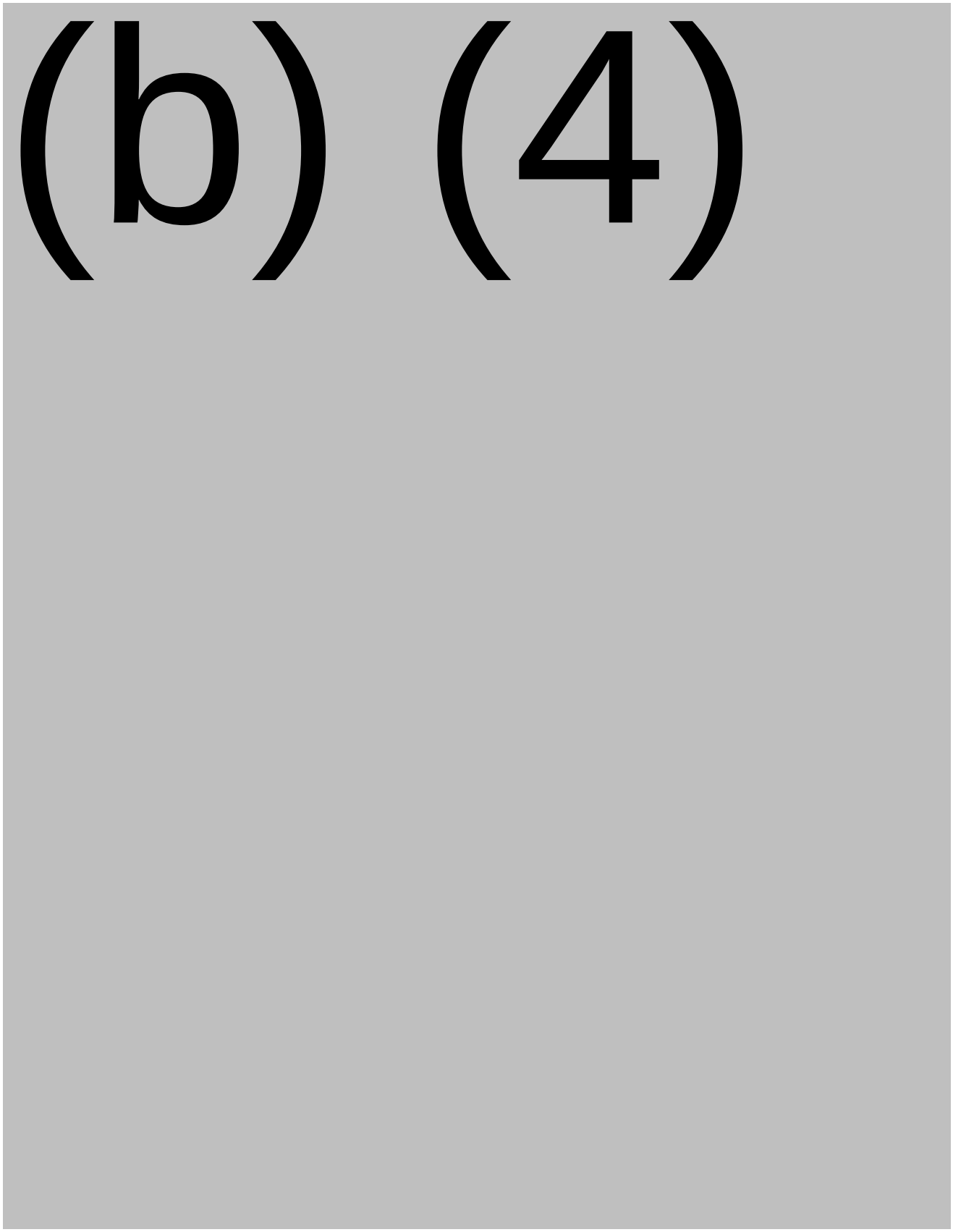
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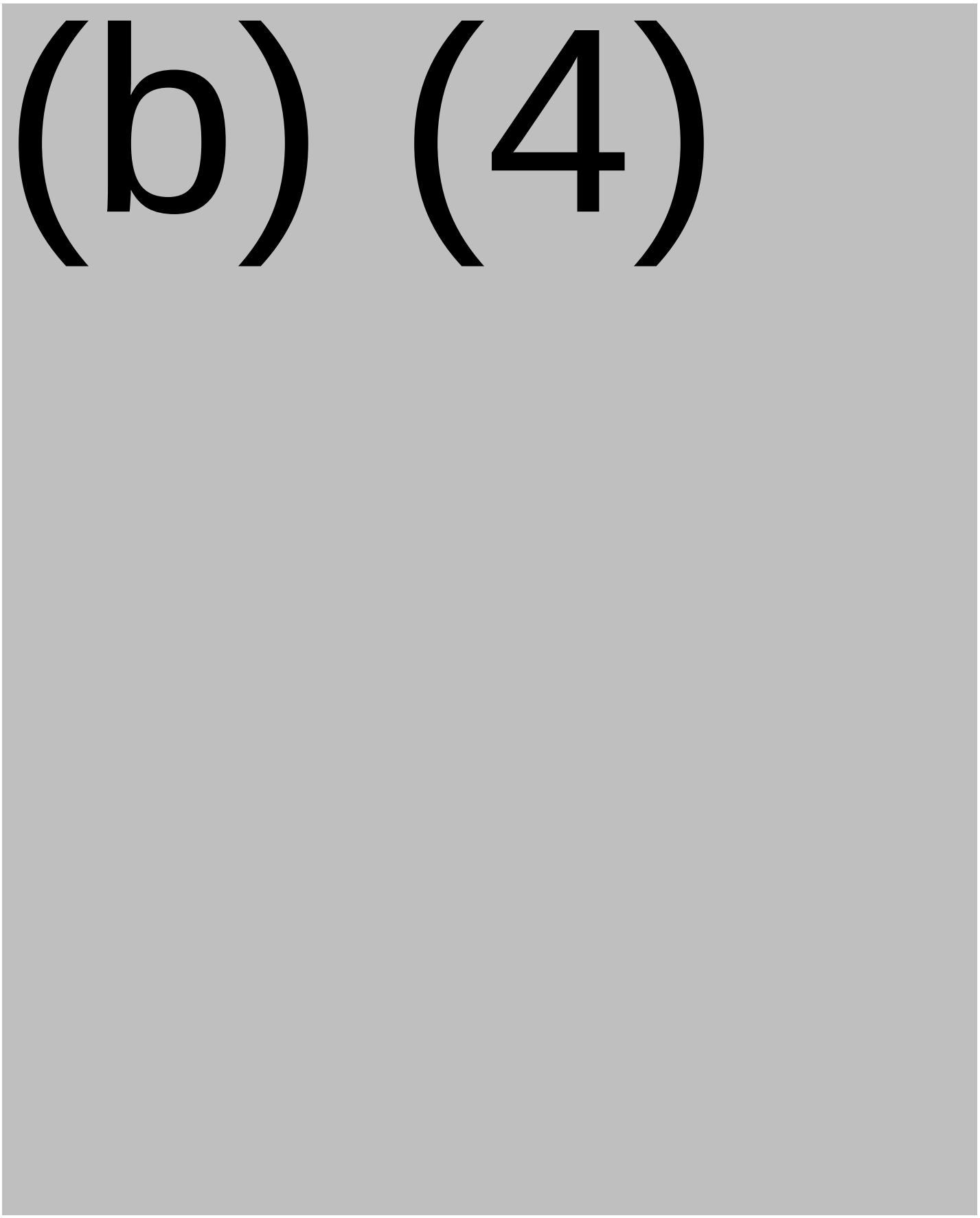
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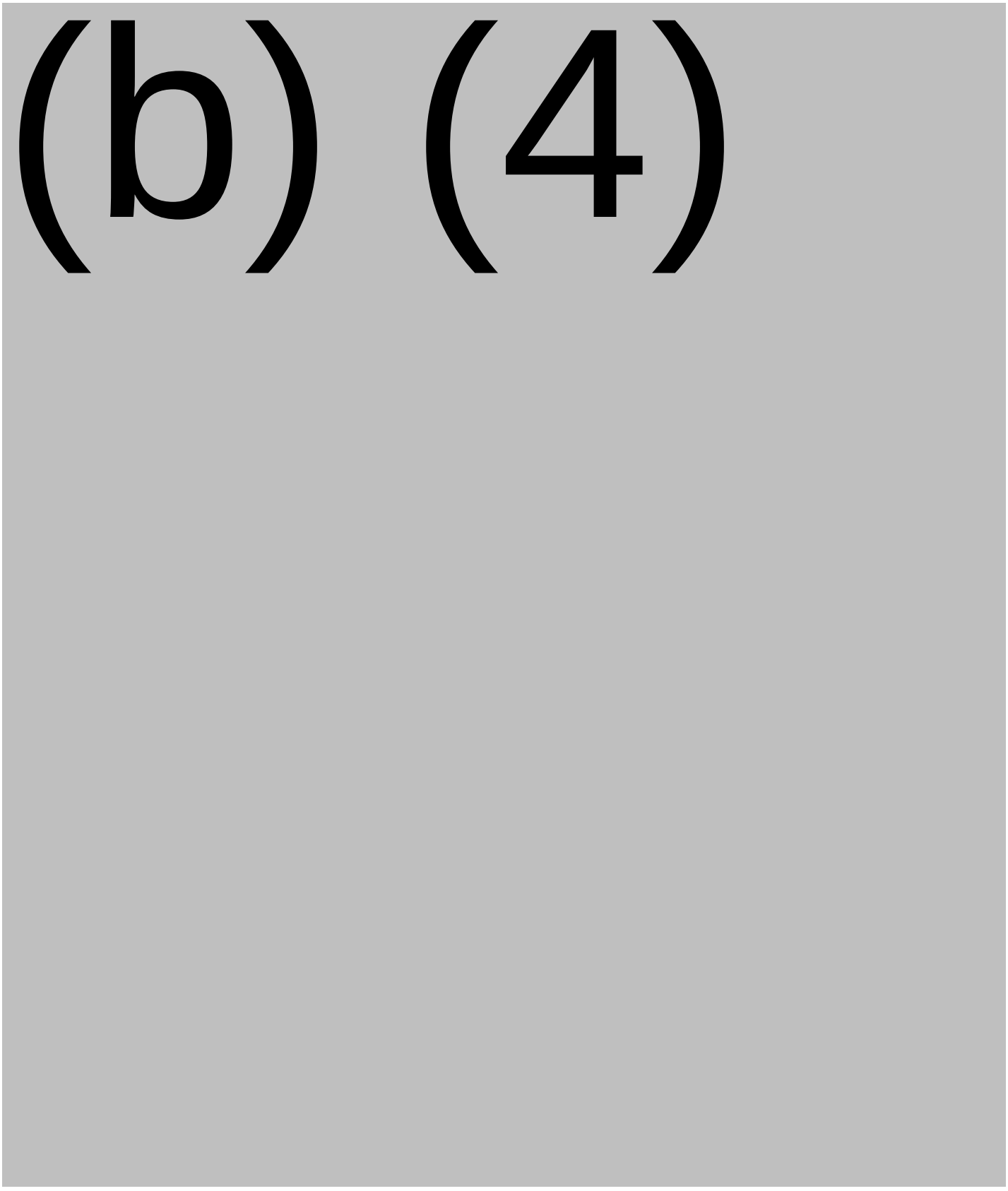
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3. History Of Use and Evidence Of Safety

3.1 History of use

3.1.1 Description of the relationship between the historically consumed material and the NDI or dietary supplement containing the NDI

The historical connection between the traditionally consumed material and Caesalpinia spinosa, or products containing this botanical ingredient, can be traced back to indigenous cultures in South America. For centuries, communities in the Andean regions of Peru, Colombia, and Ecuador have recognized the remarkable properties of Caesalpinia spinosa, commonly known as tara or tara gum. The seeds and pulp of the Caesalpinia spinosa tree have been utilized in traditional medicine and culinary practices.

In traditional medicine, indigenous populations have used Caesalpinia spinosa for its potential health benefits. It has been employed for its reported anti-inflammatory, antimicrobial, and wound-healing properties. The seeds and pulp of the Caesalpinia spinosa tree have also been included in various traditional remedies to address digestive issues and promote overall well-being.

3.1.2 Adverse events associated with historically consumed material

No adverse events were reported.

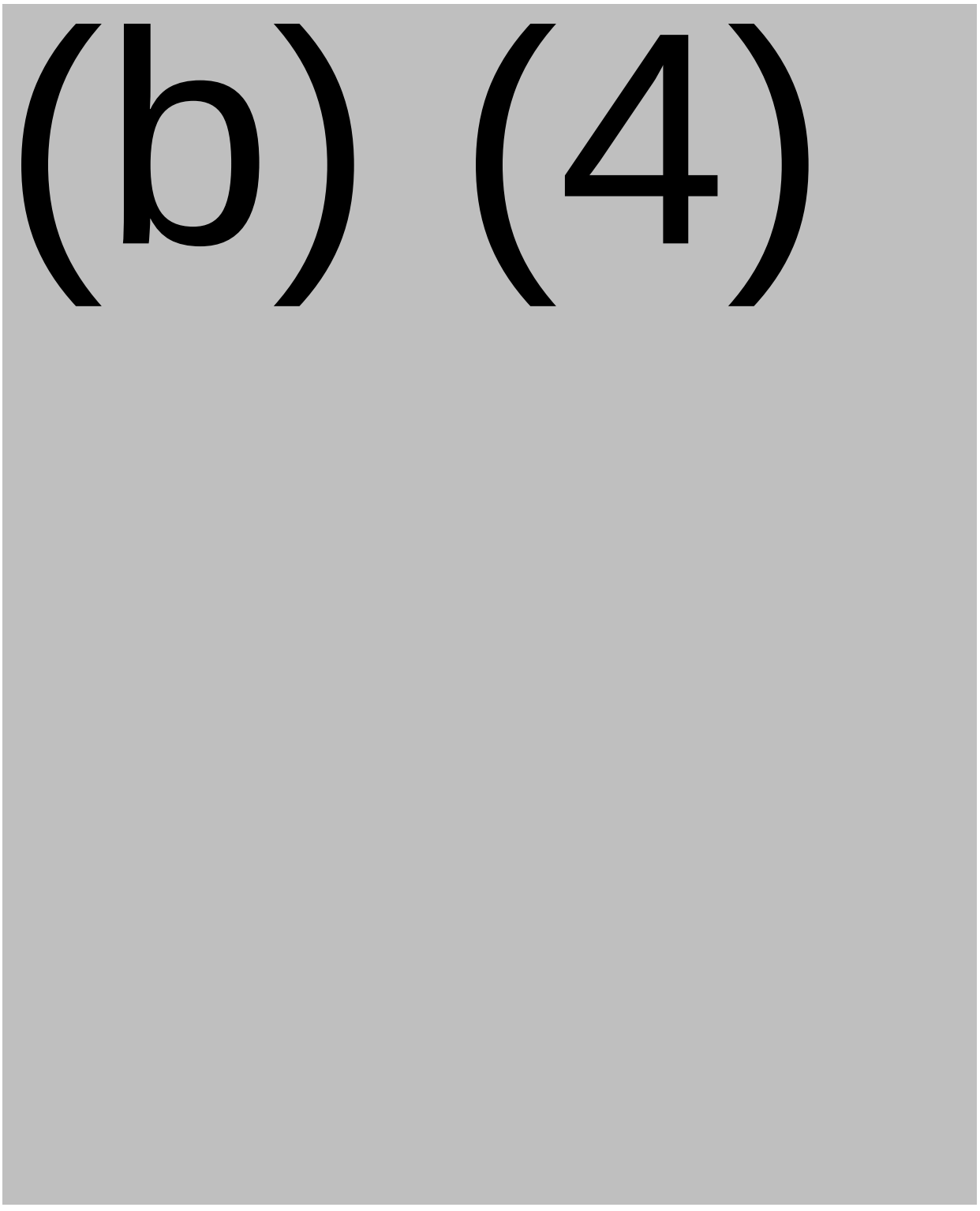
3.2 Other evidence of safety

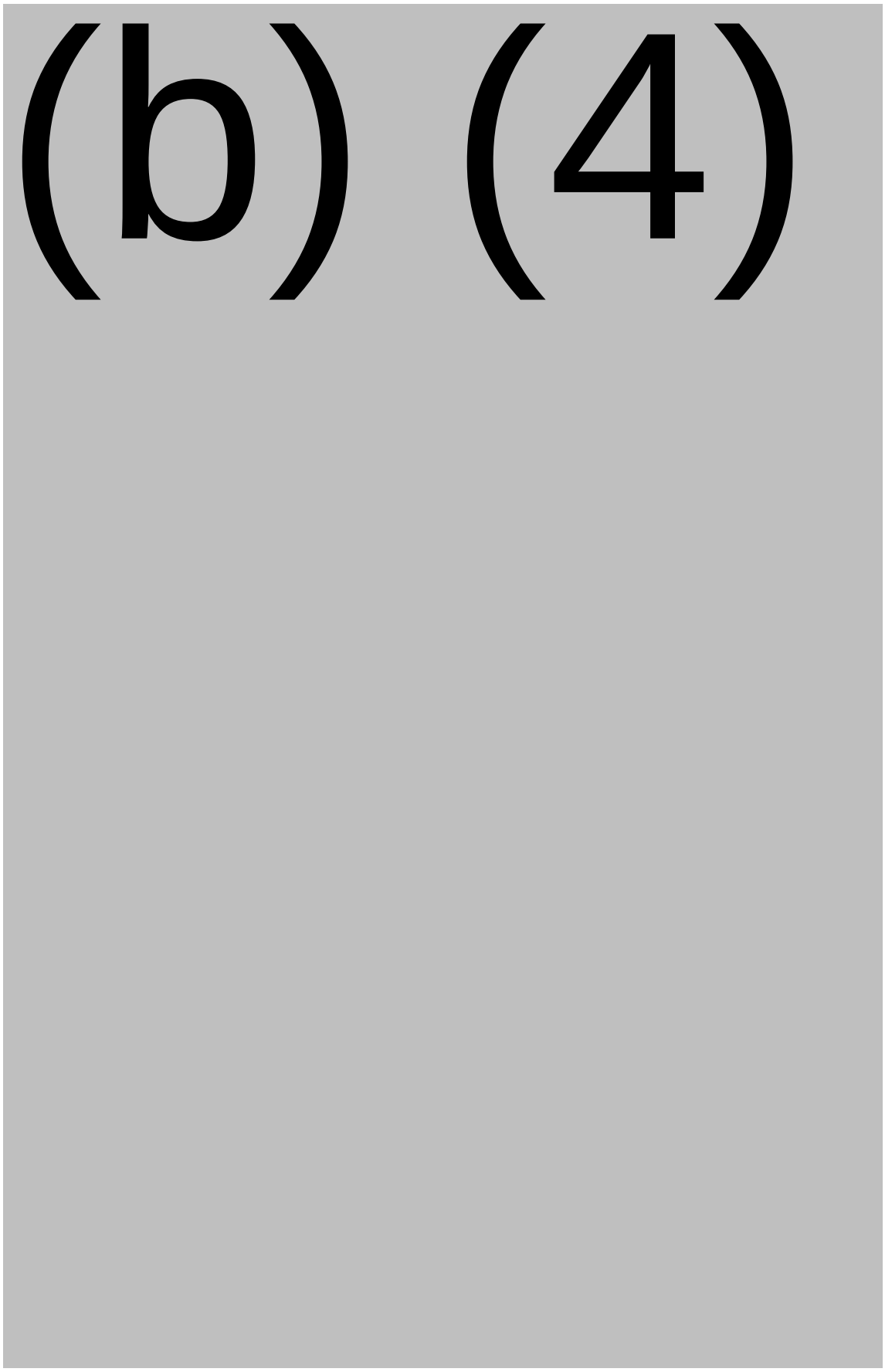
3.2.1 Safety study type

The Caesalpinia spinosa dry extract underwent the following studies:

- Ames test (Genotoxicity)
- Micronucleus test
- Oral acute toxicity
- Chronic toxicity over 180 days
- Chronic toxicity

A summary of the results from the Genotoxicity, acute, and chronic studies is provided below. The detailed findings from these studies are attached as Annexes.

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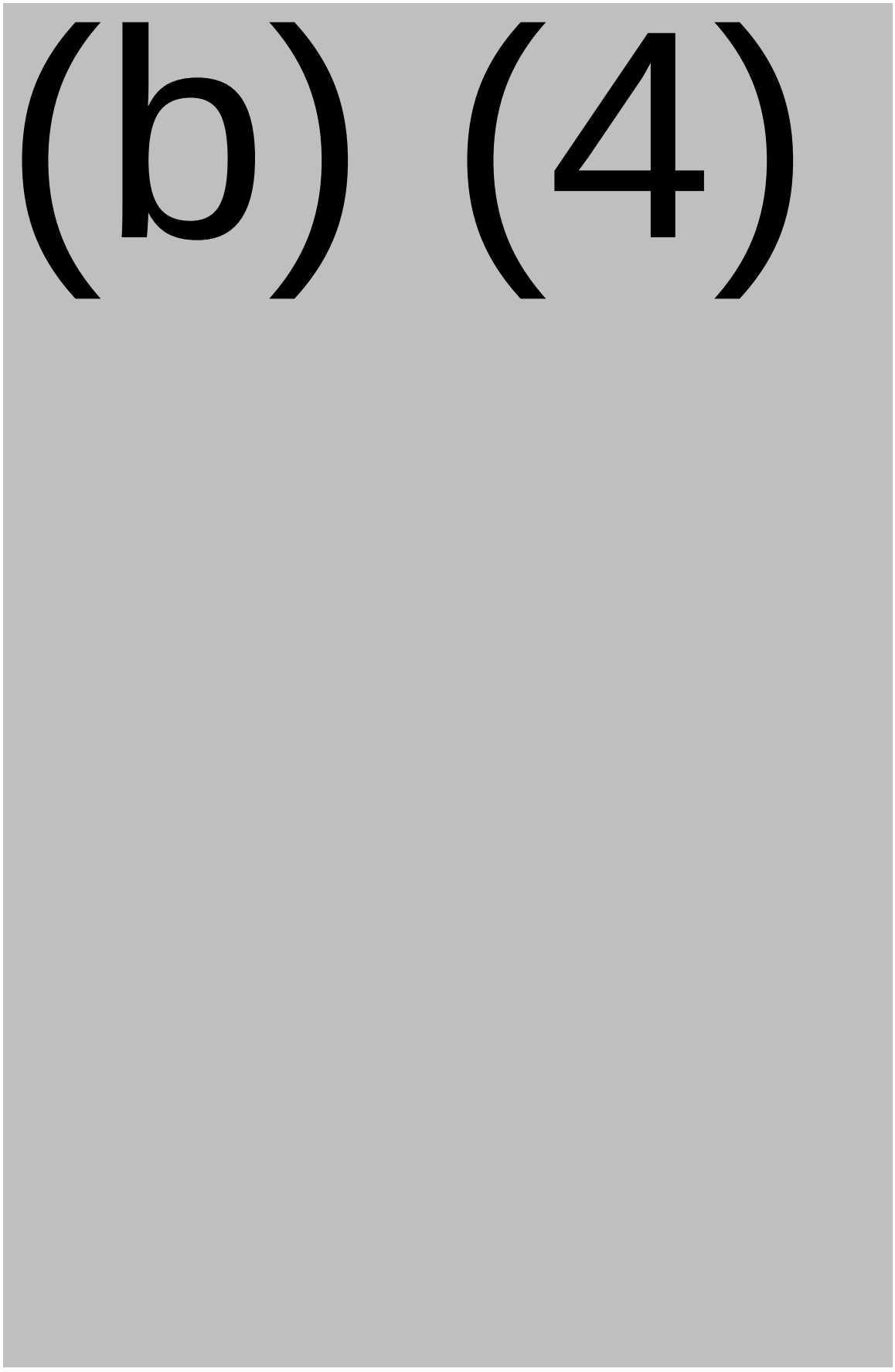
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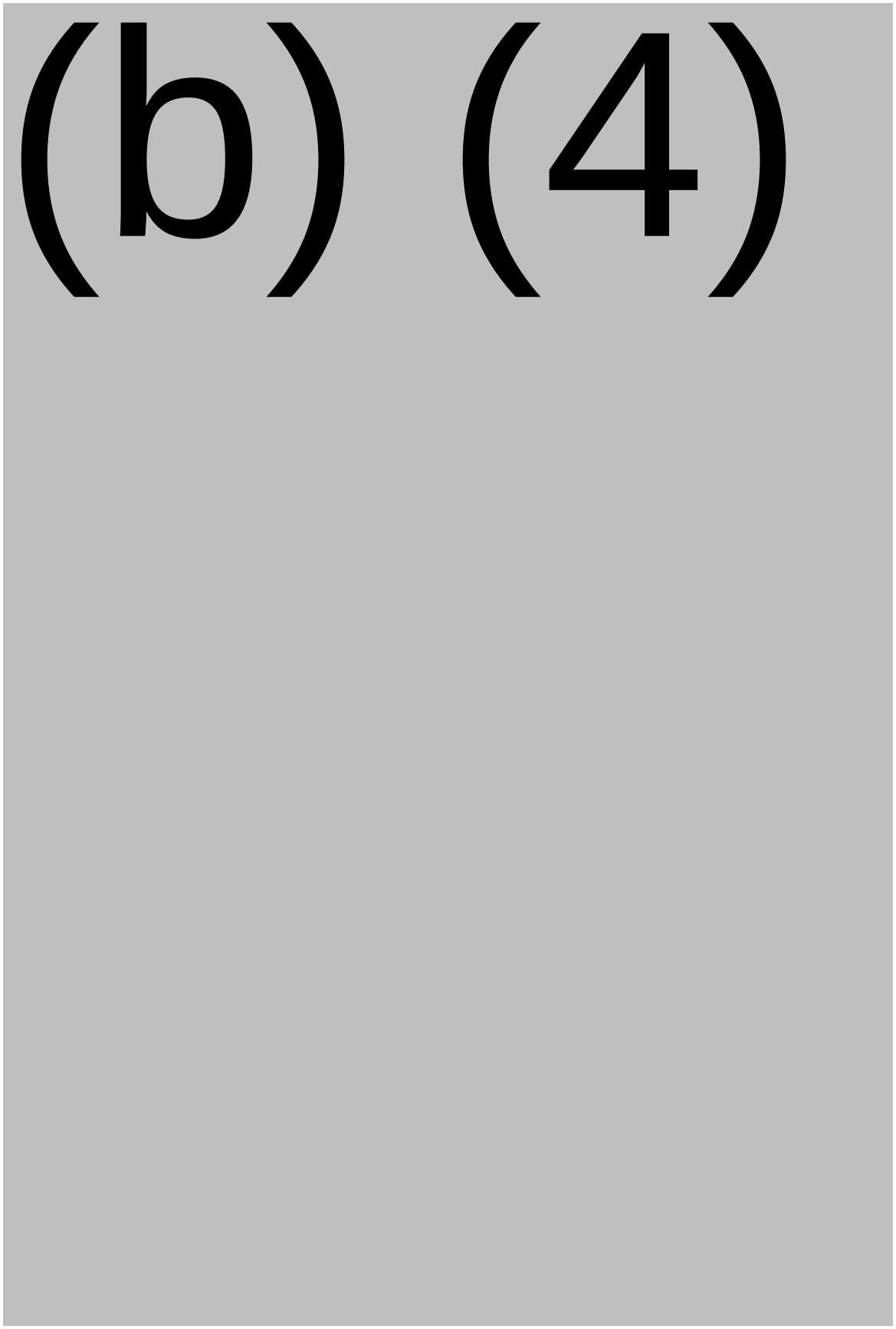
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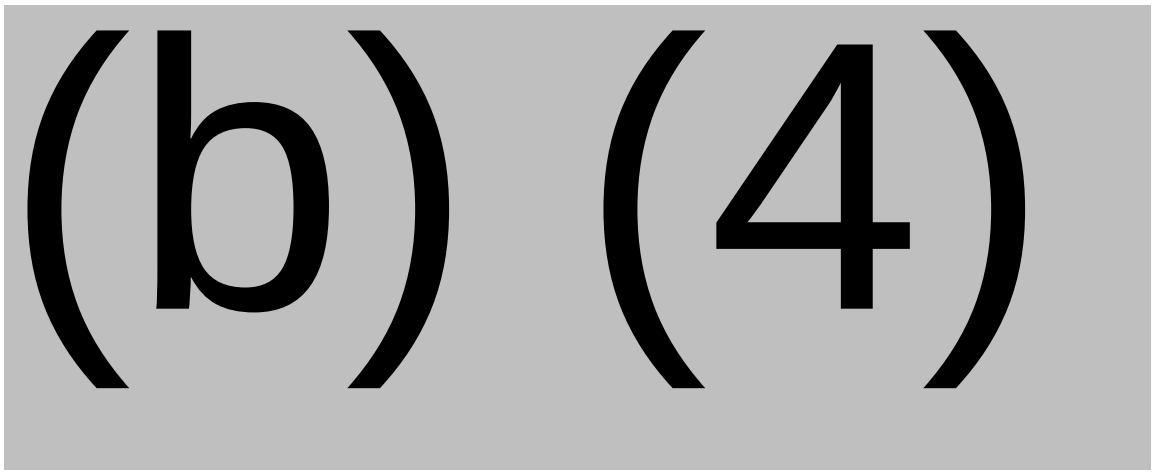
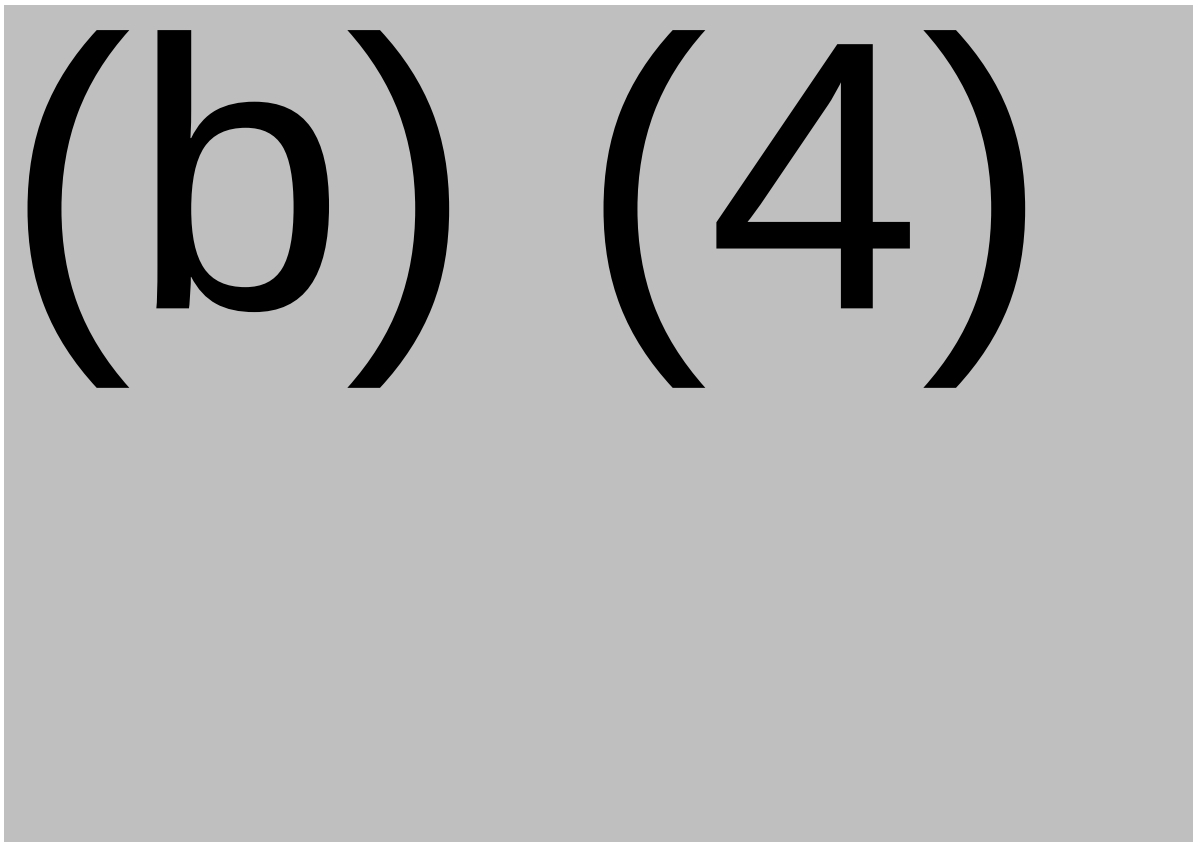
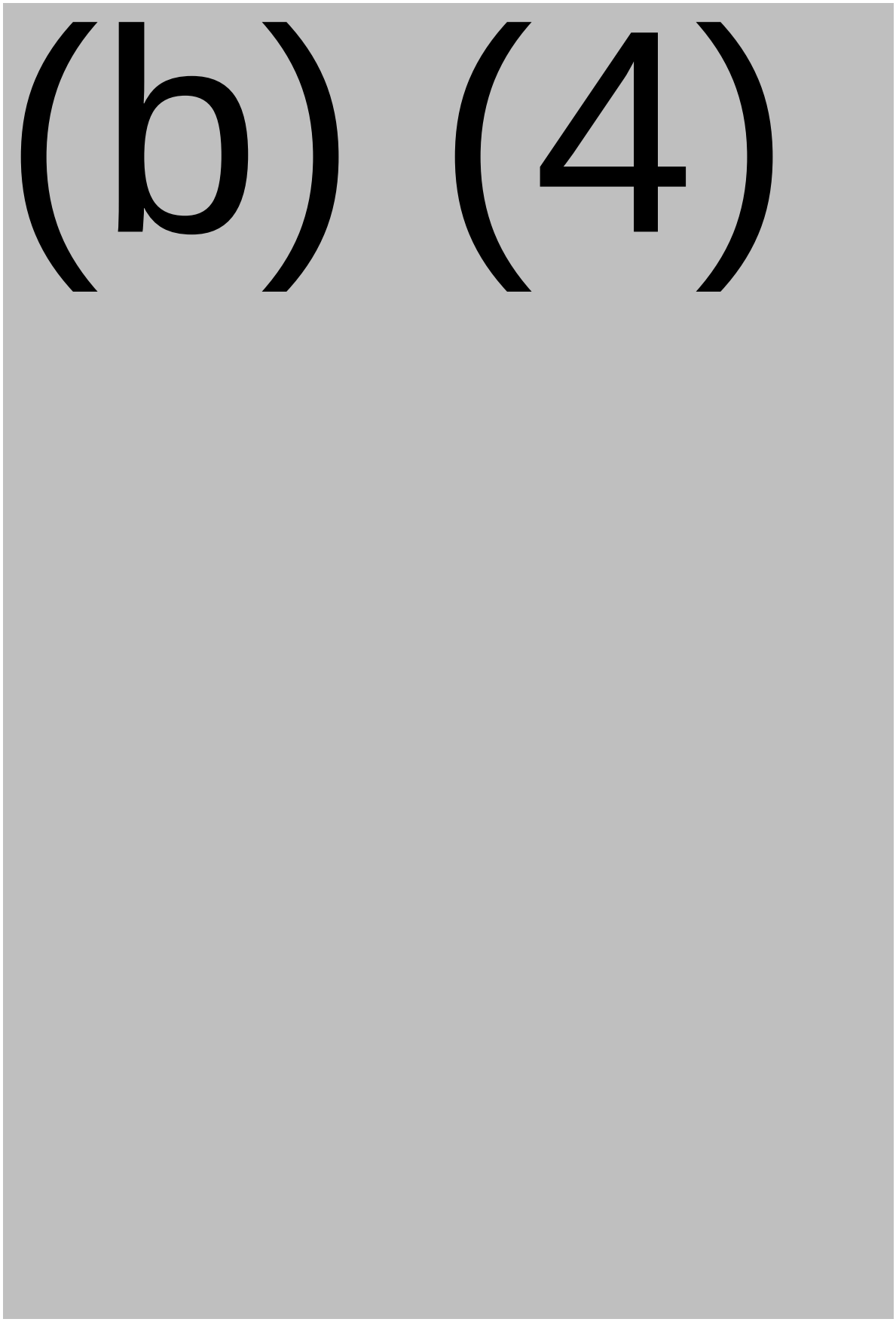


Acute and chronic studies

The following studies were conducted:

- Oral and acute toxicity:
- Determination of LD50
- Repeated dose toxicity for 28 days in rabbits
- Repeated dose toxicity for 28 days on rats
- 180-day repeated dose toxicity test Acute Oral Toxicity

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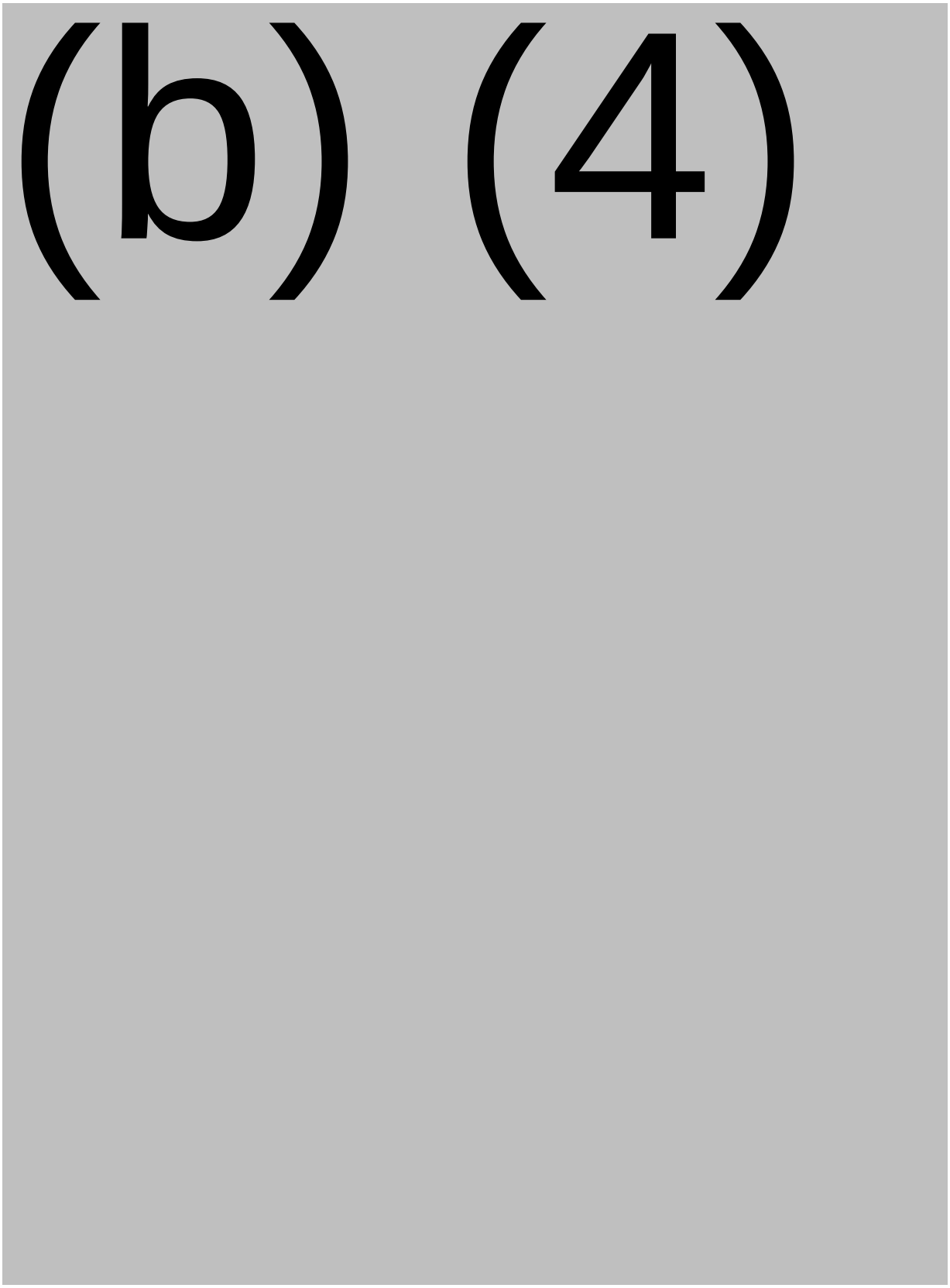
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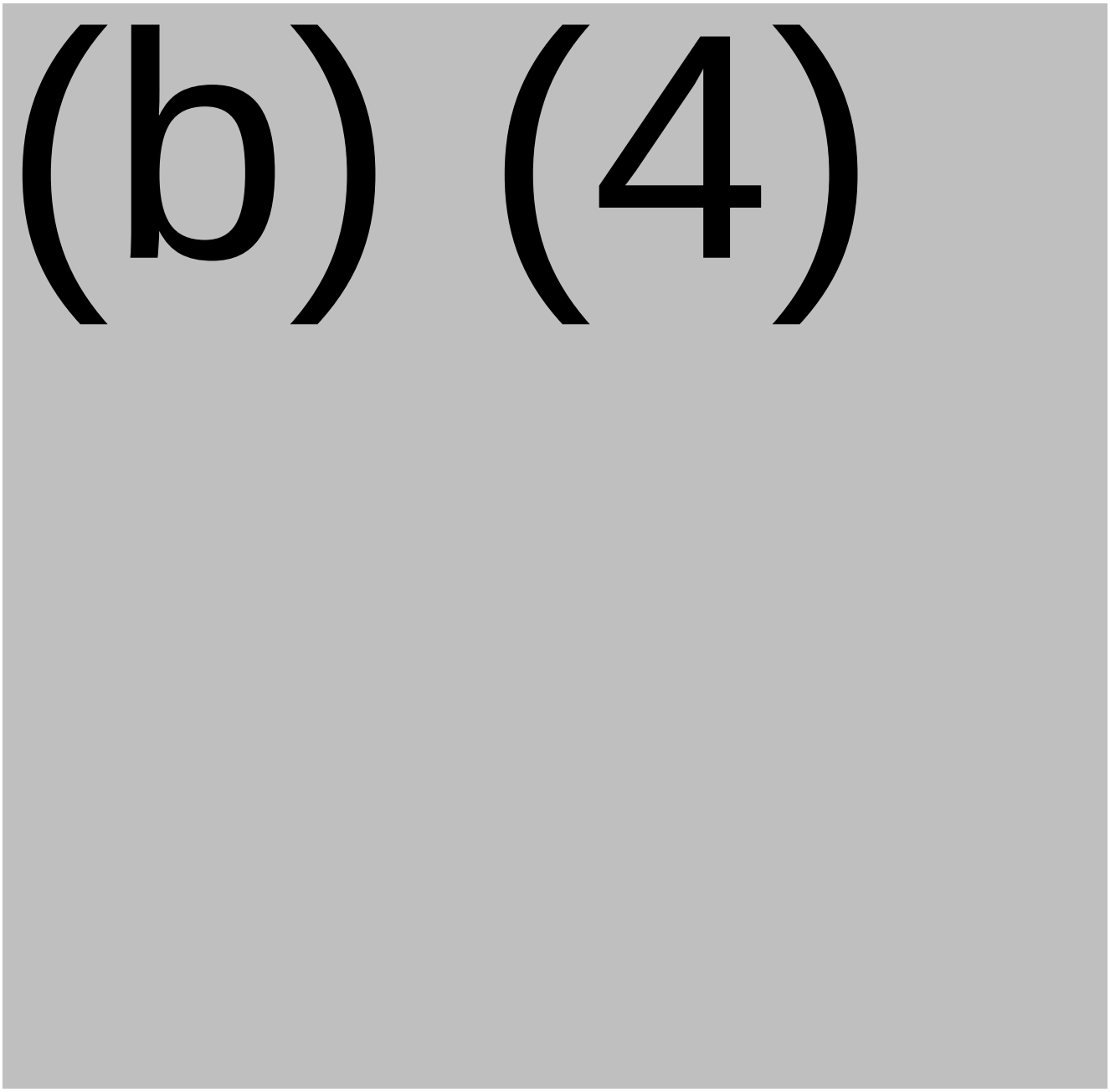
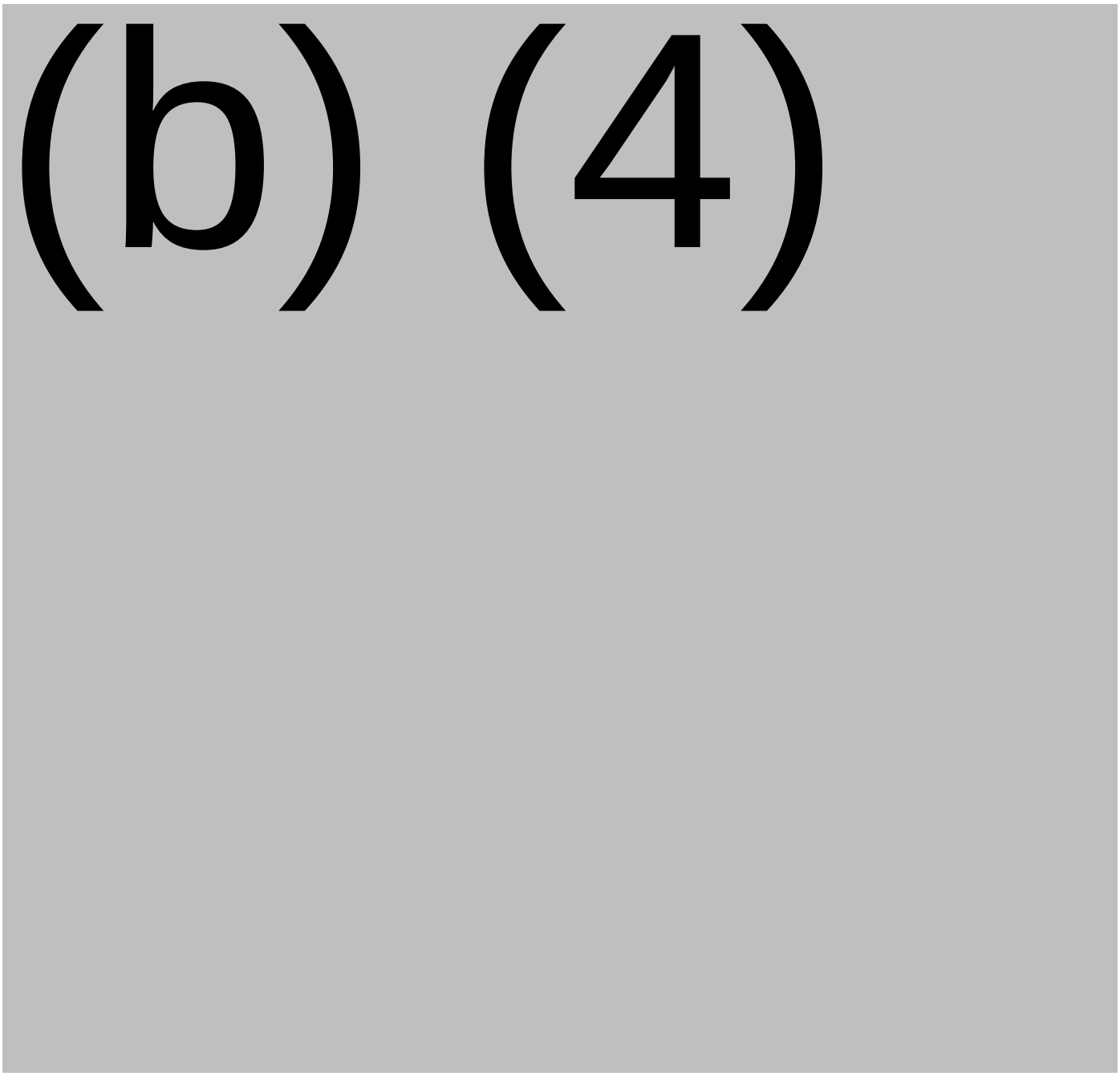
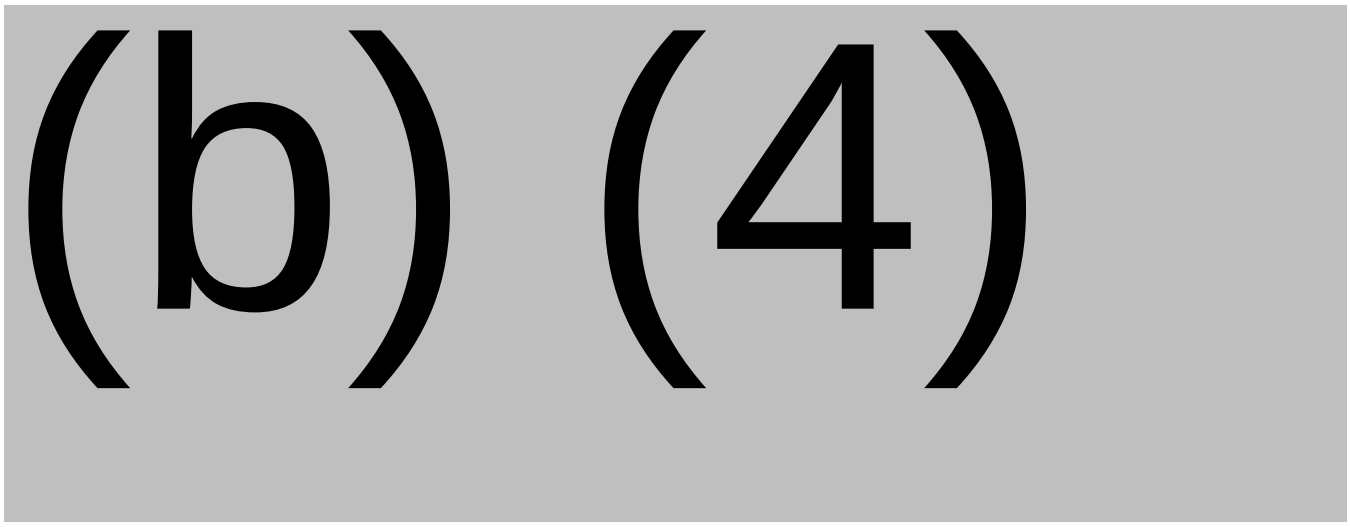
3.2.2 Discussion of toxicity and conclusion



4. Basis For Concluding That the New Dietary Ingredient Will Reasonably Be Expected To Be Safe For Use in the Dietary Supplement

4.1 Alternative basis for reasonable expectation of safety

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5. Reference List

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Duran María, Ballesteros-Ramírez Ricardo, Tellez Angélica, Torregrosa Lilian, Olejua Peter A, Galvis Silvia, Urueña Claudia, Fiorentino Susana, "Safety Evaluation in Healthy Colombian Volunteers of P2Et Extract Obtained from Caesalpinia spinosa: Design 3+3 Phase I Clinical Trial", Evidence-Based Complementary and Alternative Medicine, vol. 2022, Article ID 7943001, 11 pages, 2022. https://doi.org/10.1155/2022/7943001).

Gao J, Hu J, Hu D, Yang X. A Role of Gallic Acid in Oxidative Damage Diseases: A Comprehensive Review. Natural Product Communications. 2019;14(8). doi:10.1177/1934578X19874174

6. Annex

Results of preclinical and clinical trials