

# Letters

## RESEARCH LETTER

### Quantity of Melatonin and CBD in Melatonin Gummies Sold in the US

Prior to the COVID-19 pandemic, melatonin was used by an estimated 1.3% of children in the US, most commonly for sleep, stress, and relaxation.<sup>1,2</sup> Despite the lack of high-quality evidence to support melatonin's efficacy for these indications in healthy children, use increased during the COVID-19 pandemic. Calls for pediatric melatonin ingestions to US Poison Control

Centers increased 530% from 2012 to 2021 and were associated with 27 795 emergency department and clinic visits, 4097 hospitalizations, 287 intensive care unit admissions, and 2 deaths.<sup>3</sup>

Melatonin products are not approved by the US Food and Drug Administration (FDA). Instead, they are sold over the counter as dietary supplements or food, and some products include prohibited drugs such as cannabidiol (CBD). Given that children might intentionally or unintentionally ingest melatonin gummies, we assessed the actual quantity of melatonin and CBD in these products compared with the quantities declared on the labels.

 [Supplemental content](#)

Table. Information Provided on the Label Compared With Quantity Detected of Melatonin and CBD in Analyzed Samples of Melatonin Gummies

Brand code	Label claims	Expiration date	Labeled quantity of ingredients per serving size	No. of other ingredients <sup>a</sup>	Label maximum daily servings, No. of gummies	Measured ingredients per serving size (SD), mg	Measured vs labeled ingredients per serving size, %
A	Circadian rhythm support	06/2024	Melatonin, 3 mg CBD, 10 mg	2	1	Melatonin: 3.6 (0.7) CBD: 10.6 (0.5)	Melatonin: 120 CBD: 106
B	Heartburn relief plus sleep support	01/2024	Melatonin, 3 mg	0	2	4.8 (0.3)	160
C	Occasional sleeplessness	09/2023	Melatonin, 5 mg	0	2	6.1 (0.2)	122
D	Rest and rejuvenate	03/2023	Melatonin, 5 mg	1	2	3.7 (0.4)	74
E	Night calm	02/2024	Melatonin, 3 mg	3	2	4.5 (0.3)	150
F	Sleep	08/2024	Melatonin, 5 mg CBD, 15 mg	0	2	Melatonin: 6.6 (0.2) CBD: 15.8 (0.1)	Melatonin: 132 CBD: 105
G	Sleep	08/2024	Melatonin, 5 mg CBD, 15 mg	0	2	Melatonin: 7.2 (0.3) CBD: 17.7 (1.0)	Melatonin: 144 CBD: 118
H	Sleep	05/2023	Melatonin, 5 mg CBD, 15 mg	0	2	Melatonin: 4.7 (0.1) CBD: 16.1 (0.2)	Melatonin: 94 CBD: 107
I	Sleep support	08/2024	Melatonin, 5 mg CBD, 30 mg	0	2	Melatonin: ND CBD: 31.3 (1.1)	Melatonin: ND CBD: 104
J	No claim	06/2023	Melatonin, 5 mg	0	2	6.0 (0.1)	120
K	No claim	12/2023	Melatonin, 3 mg	1	2	4.6 (0.3)	153
L	Healthy sleep cycle support	02/2024	Melatonin, 5 mg	0	2	5.9 (0.3)	118
M	Supports healthy sleep	11/2023	Melatonin, 5 mg	0	1	7.3 (0.1)	146
N	Supports healthy sleep	02/2024	Melatonin, 10 mg	0	2	13.1 (0.1)	131
O	No claim	10/2023	Melatonin, 5 mg	0	2	5.4 (0.4)	108
P	No claim	09/2023	Melatonin, 3 mg	1	2	5.1 (0.8)	170
Q	Rest and restore muscles	08/2023	Melatonin, 3 mg	2	2	4.0 (0.3)	133
R	No claim	02/2024	Melatonin, 3 mg	2	2	3.8 (0.1)	126
S	Sleep plus immune	09/2023	Melatonin, 3 mg	5	2	10.4 (0.4)	347
T	No claim	05/2024	Melatonin, 2.5 mg	0	1	2.9 (0.3)	116
U	No claim	07/2023	Melatonin, 1.0 mg	0	1	1.3 (0.4)	130
V	Sleep support, wake-up	10/2023	Melatonin, 10 mg	3	2	9.2 (0.3)	92
W	Supports restful sleep	09/2023	Melatonin, 5 mg	0	2	5.8 (0.6)	116
X	No claim	09/2023	Melatonin, 5 mg	0	2	5.7 (1.3)	114
Y	Sleep health	07/2023	Melatonin, 3 mg	1	2	3.7 (0.2)	123

Abbreviations: CBD, cannabidiol; ND, not detected where limit of detection is 100 ng/mL.

<sup>a</sup> Other ingredients declared included extracts of lemon balm, passionflower,

tart cherry fruit, magnolia, *Griffonia simplicifolia*, wild blueberry, black elderberry, and chamomile flower as well as collagen, L-theanine, vitamin C, and vitamin D.

**Methods** | In September 2022, products formulated as gummies with “melatonin” on the label were identified in the National Institutes of Health’s Dietary Supplement Label Database, the most comprehensive database of dietary supplements sold in the US.<sup>4</sup> The 30 unique brands entered into the database in 2021 were purchased online. Products’ labels were examined after purchase and excluded if “melatonin” did not appear on the actual label.

Gummies from the supplement products were reconstituted in methanol and an aqueous mixture of acetonitrile-methanol and then analyzed for the presence and quantity of melatonin, CBD, and serotonin using ultra high-performance liquid chromatography-photodiode array analyses (see the eAppendix in [Supplement 1](#) for details of the laboratory methods and their validation). Screening for serotonin was performed as serotonin has previously been found as a contaminant in melatonin products.<sup>5</sup>

**Results** | Of the 30 melatonin gummy brands meeting the inclusion criteria, 4 were unavailable for purchase and 1 did not contain “melatonin” on the actual label; therefore, 25 products were analyzed. One product did not contain detectable levels of melatonin but did contain 31.3 mg of CBD. In the remaining products, the quantity of melatonin ranged from 1.3 mg to 13.1 mg per serving size ([Table](#)). In products that contained melatonin, the actual quantity of melatonin ranged from 74% to 347% of the labeled quantity. Twenty-two of 25 products (88%) were inaccurately labeled, and only 3 products (12%) contained a quantity of melatonin that was within  $\pm 10\%$  of the declared quantity. Five products declared CBD as an ingredient, and the quantity of CBD ranged from 10.6 mg to 31.3 mg per serving. The actual quantity of CBD ranged from 104% to 118% of the labeled quantity. Serotonin was not detected in any product.

**Discussion** | The great majority of melatonin gummy products were inaccurately labeled, with most products exceeding the declared amount of melatonin and CBD. To our knowledge, this is the first US study to quantify melatonin in over-the-counter melatonin products. A Canadian study had similar results: analysis of 16 Canadian melatonin brands found that the actual dose of melatonin ranged from 17% to 478% of the declared quantity.<sup>5</sup>

Administration of as little as 0.1 mg to 0.3 mg of melatonin to young adults can increase plasma concentrations into the normal nighttime range.<sup>6</sup> Consuming melatonin gummies as directed could expose children to between 40 and 130 times higher quantities of melatonin. Unintentional ingestions could lead to consumption that greatly exceeds these dosages of melatonin. With respect to CBD, the drug is FDA approved to treat refractory seizures caused by 3 rare genetic disorders, but the FDA has not approved the use of CBD for any indication in healthy children.

This study has limitations, including that the sample size was small, only 1 sample of each brand was analyzed, and only gummies were analyzed. It is not known if the results are generalizable to melatonin products sold as tablets and capsules in the US or if the quantity of melatonin within an individual brand may also vary from batch to batch.

Given these findings, clinicians should advise parents that pediatric use of melatonin gummies may result in ingestion of unpredictable quantities of melatonin and CBD.

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**Concept and design:** Cohen, Khan.

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**Data Sharing Statement:** See [Supplement 2](#).

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## Trends in Buprenorphine Initiation and Retention in the United States, 2016–2022

Increasing initiation of therapy with buprenorphine, a highly effective medication for opioid use disorder, is important in light of record US opioid-related mortality.<sup>1,2</sup> Ensuring retention in therapy after buprenorphine initiation is also important because retention is strongly associated with decreased opioid-related mortality.<sup>3</sup>