

# Infant sleep and the use of common remedies: A case report

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## Abstract

**Background:** The rate and variety of use of common therapies to treat illness in different countries are quite different. Moreover, use of these therapies in infants and children is even more obscure. Unfortunately, these therapies are unstudied and unregulated. Little is known about the efficacy and more importantly the safety of such products. In this report we present the case of an infant who was supplemented with a product called Sleep Drops<sup>®</sup> which is marketed to be safe and effective.

**Case report:** this is a case of a 6-month healthy infant who has trouble sleeping. Her mother gave her Sleep Drops<sup>®</sup> product at an increasing amount for a couple of nights. The infant to be more agitated than usual during the day and her sleep pattern became more erratic and became drowsy at times and fell asleep faster at the beginning of the night. The mother sought advice from the community pharmacist because she is not happy with outcome of sleep drops and seeking other treatment for her infant to help her sleeping.

**Conclusion:** Further analysis as to the content of the product reveals that it contains pharmacologically active substances that might cause serious side effects. In the future more, studies are needed to determine safety profile of these remedies. Presently, stricter regulations and more awareness are needed to protect the public from inappropriate use and possible dangerous consequences. The mother sought advice from the community pharmacist because she is not happy with outcome of sleep drops and seeking other treatment for her infant to help her sleeping.

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## Introduction

Newborn children do not have a developed circadian rhythm and subsequently rest over different intervals for the duration of the day and night in short sessions, which may also be due to infants' feeding needs. The circadian rhythm starts developing at the age of 10-12 weeks, when an infant starts to be able to sleep through the night. Through the first year, the need for day sleep decreases while night sleep duration increases [1].

Despite the general trend of decrease in Day time sleeping period, night awakenings show the highest levels of variability. The National Sleep Foundation (NSF) recommends a daily sleep duration of 14-17 hours/day from birth to 3 months, 12-15 hours/day from 4 to 11 months, 11-14 hours/ day for infants aged 1-2 years, and 10-13 hours/day for preschoolers aged 3-5 years [2].

Variation in infant sleep play has an important role in cognitive development and physical growth. Studies on cognition show that individual differences in sleep quantity and quality are particularly important for the development of memory, language, and executive functions. Studies on physical growth indicate the potential risk of sleep problems, in particular shorter sleep duration early in life, for overweight, obesity, or measures of adiposity in infants, toddlers, and preschool-age children [1].

The Consensus Statement of the American Academy of Sleep Medicine (CSACSM) summarized key evidence related to the panel

found that sleeping the recommended hours regularly is associated with better health outcomes including improved attention, behavior, learning, memory, emotional regulation, quality of life, and mental and physical health. Regular lack of enough sleep during early childhood is linked to attention, behavior, and learning problems. Inadequate sleep also increases the risk of accidents, injuries, hypertension, obesity, diabetes, and depression. Insufficient sleep in teenagers is associated with increased risk of self-harm, suicidal thoughts, and suicide attempts [3].

The rate and variety of using common therapies to treat illness in different countries are quite different. (Fesharakinia & Abedini 2014) Despite relatively little is known about why people seek common sleep remedies before conventional medical treatment, the use of common sleep remedies may be attributed to personal preference or choice and beliefs about the health benefits of these remedies [4]. Individual's personal characteristics age, education, perceived control over health

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and spirituality significantly predicted intention to try common sleep remedies [5,6].

An increasing number of parents are using complementary therapies to induce sleeping to their children. There is still insufficient data to determine the safety profile of these therapies, nonetheless, mothers believe that these therapies are natural and thus safe [7]. Parents of new-borns and infants suffer from lack of sleep due to the erratic sleep patterns of their youngsters. This lack of sleep leads to fatigue in the parents and in turn causes them to seek different solutions including quick fixes such as over the counter antihistamines or cough syrups. Some parents resort to alternative or herbal therapies due to the false belief that these “natural” products are safer. Examples include melatonin, chamomile, lemon balm, and commercial products such as Sleep Drops®, Bioray Inc., NDF Sleep®.

Sleep Drops® is marketed through Sleep drops International and is sold through many commercial websites [8-10]. Different products are available for adults, kids and infants’ babies. The company claims that the products are aimed to target toddlers from 0-3 years and 3-12 years of age and claim to produce the following benefits [11]:

- Supports for your babies or toddlers getting to sleep and staying asleep!
- Support for a calm and happy baby due to additional support for common complaints such as teething or colic, that can cause your little one to be unhappy
- Support for “tummy” issues
- More sleep for you as a parent
- Total confidence, knowing you are giving your infant a natural formula
- More “me time” for you, as you spend less time calming a distressed little one

The products list the following ingredients:

“Organic Coconut Glycerine, purified water, ethanol, *Corydalis ambigua* (*Corydalis*), *Eschscholzia californica* (Californian poppy), *Humulus lupulus* (Hops), *Lavandula officinalis* (Lavender), *Matricaria recutita* (Chamomile), *Passiflora incarnate* (Passionflower), *Piper methysticum* (Kava), *Scutellaria baicalensis* (Baical Skullcap), *Albizia lebeck* (*Albizia*), *Viburnum opulus*, (Cramp bark) *Zizyphus jujuba* (*Zizyphus*) with Homeopathic Calc phos, *Chamomilla*, *Colocynthis*, *Kreosotum*, Mag phos, combined with flower essences.”

Closer examination of the product revealed that it is marked as an herbal product thus food supplement and therefore concentrations of each ingredient and constituent are not listed. In addition, one of the listed ingredients is ethanol, in unknown concentration. Both these facts should raise significant issues for any healthcare provider.

## Case report

A 6-month infant girl does not sleep well at night since the past 14 days. She keeps waking up every hour or so, as described by her parents. She also seems agitated throughout the day because she doesn’t get enough sleep at night. The working mother is not able to get her needed rest and therefore seeks a solution for her dilemma. The mother sought to find helpful information on the internet through blogs and discussion boards, and she has found numerous accounts of experience with the product Sleep Drops® [12-14]. She tried this product with her infant using 3-4 drops in the evening for the last couple of days,

because the recommended dose of one drop was not effective. The mother noticed her infant to be more agitated than usual during the day and her sleep pattern became more erratic although the infant seemed drowsy at times and fell asleep faster at the beginning of the night. The mother sought advice from the community pharmacist because she is not happy with outcome of sleep drops and seeking other treatment for her infant to help her sleeping. The mother admits she obtained the product through a seller she found on social media. The pharmacist researched about this product and the ingredients in it. She advised the mother to stop using it since it contains some ingredients that might be unsafe for the infant and advised the mother to visit her pediatrician.

The mother visited the pharmacist again later the same day, to report that the infant was examined and is well and healthy. It has been more than 24 hours since the last dose and there seems to be no residual effect of the sleep Drops®. The pharmacist spent time with the mother to educate her against buying products from unknown sources and the dangerous of using such products especially in infants.

## Discussion

At the clinic, examinations failed to find any health issues with the infant that could explain the restless sleep pattern except the infant being in the early teething stage. The mother and infant were referred to the nurse to educate the mother on strategies to use to help with infant sleep problems and complications of teething. Additionally, the mother was referred to the pharmacist to go over what remedies and non-prescription medication that can or cannot be used safely for this infant.

When analyzing the suggested method of administration, the Sleep Drops® product states that “drops are to be put under the tongue, or close to the tongue and lips, inside the mouth” [15]. This indicates that the route of administration is not through ingestion, but it is through sublingual or buccal administration, which is considered as a major route of administration that by-passes the first pass hepatic metabolism [16]. Therefore, this route of administration has a direct access to the bloodstream and hence rapid onset of action. Moreover, since the concentration of ingredients is unknown and hence their bioavailability, the response can be very rapidly serious and hugely concerning [17].

Previous studies revealed the mechanism of action by which some of this product’s herbal ingredients can induce sleep.

### *Corydalis ambigua* (*Corydalis*)

The chemical compound called dehydrocorybulbine (DHCB) extracted from this herb provides analgesia and hypnosis through its action on central opioid receptors, in addition to its effect on cerebral D2 receptors; a mechanism by which antipsychotic drugs exert their actions [18-21].

### *Eschscholzia californica* (Californian poppy)

This herb was shown to induce hypnosis by acting on central benzodiazepine receptors [22,23]. According to the European Medicine Agency (EMA), the use of this herb is restricted for clearly diagnosed anxiety for individuals  $\geq 12$  years of age and under medical supervision [24].

### *Humulus lupulus*

Like Californian poppy, according to EMA, this herb is not allowed to be used for individuals <12 years of age and its usage should be under careful medical supervision for those individuals who are

diagnosed with anxiety (16,17). Additionally, pharmacological studies revealed that this herb's extract induces hypnosis through its action on melatonin receptors in addition to benzodiazepine receptors [25,26].

### Piper methysticum (Kava)

In 2001, EMA issued a report of caution regarding the use of this herb after numerous cases of acute hepatitis were reported across the world [27-30]. Accordingly, the FDA and a recent study have issued a warning that this herb should be used under careful medical supervision [30-35].

Moreover, clinical studies all of which are conducted on adults revealed the ability of this herb to bind with benzodiazepine receptors and hence induce hypnosis [36,37].

### Scutellaria baicalensis

According to pharmacological studies, this herb is capable of inducing hypnosis through benzodiazepine pathway [38-40]. Moreover, according to the FDA, the use of this product is restricted to individuals  $\geq 12$  years of age [41].

### Albizia lebbek

Numerous pharmacological studies revealed the ability of this herbal extract to induce hypnosis through benzodiazepine pathway, blocking H1-receptors and 5-HT pathway, in addition to a mechanism that is similar to barbiturates [42-45].

### Ethanol

The product also contains ethanol which is a CNS depressant [46]. Ethanol may be found in a list of excipients of preparations used for infants and children. It can be harmful either for possible acute toxicity after accidental overdose or for potential chronic toxicity, with prolonged medicinal exposure for treatment of pediatric chronic diseases [47]. Ethanol in children may alter the state of consciousness, hypoglycemia, acidosis and electrolyte abnormalities [48].

Accordingly, in order to avoid potentially serious adverse effects, it was established that ethanol content in pediatric drugs should not be able to produce a blood concentration higher than 25 mg/100 ml, after the administration of a single recommended therapeutic dose [47]. Since Sleep Drops® is unregulated and unstudied it is difficult to determine the ethanol content and therefore the safety of the product.

There is a lack of formal studies on Sleep Drops® products and the scarce information available is from commercial website or blogs of past users. Consequently, there is a lack of efficacy and safety data.

### Conclusion

All ingredients described above are capable of inducing sleep through a combination of mechanisms including modulation of central D2-receptors, central benzodiazepine receptors, opioid mu receptors, melatonin, H1-receptors, and barbiturates. Therefore, considering the use of these herbs in infants raises severe health concerns especially when there is a probability of causing dependence, interference with circadian rhythm, interaction with other antihistaminic medications, and the risk of respiratory depression. Given that this product is still marketed as a dietary supplement but has marked therapeutic claims, it is important to have sufficient clinical safety and efficacy evidences before its inappropriate use. Moreover, the ingredients listed here have definite pharmacological effects that can be harmful for pediatric subjects. In addition to the safety issue, the use of these products

is unregulated because it is sold over commercial websites and local merchants over social media platforms such as Instagram and Twitter make them easily accessible.

### Recommendations

Common or complementary products like Sleep Drops® are freely available even though they contain pharmacologically active substances that act centrally to induce sleeping. Implementation of strict guidelines and regulation for their use is needed. In addition, public need to be aware and educated that common herbal remedies and non-prescription products does not mean they are always safe for everyone.

Studies are needed to identify similar use in parents from across Saudi Arabia in order to determine the magnitude of the problem and devise possible solutions.

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