

# Open label prospective study to assess the efficacy of the wake promoting beverage "WakeUp®" on vigilance and function of healthy volunteers in the morning and in the evening

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## ABSTRACT

Daytime somnolence results in a huge burden on health and function. Numerous studies have shown that daytime sleepiness results in an increased rate of accidents, poor function, reduced creativity and productivity at work, and increased health care utilization (CITATION). Previous studies have shown that consuming the herbal wake-promoting drink WakeUp® following lunch resulted in substantial improvement in alertness and function. In all previous studies, volunteers drank one bottle of the beverage (100 ml) after lunch. The purpose of the current study is to examine whether this vigilance and performance improvement remains or changes when participants drink 2 bottles per day: one in the morning and one in the afternoon/evening. Fifteen healthy volunteers (8 females) were recruited for the study. All were tested twice in the same day: once in the morning and once in the evening. Each time, they underwent a battery of tests prior to and 30 minutes following drinking 1 bottle (100 ml) of WakeUp. The battery of tests consisted of measurements of vital signs and validated, commonly used standard function and vigilance tests such as an immediate word recall test (iWRT, short term memory), digit symbol substitution test (DSST, concentration), and a subjective rating (on a visual analogue scale - VAS) of their vigilance, ability to focus, and effectiveness at work. The mean age, height, and weight of the participants were 39 years, 169 cm, and 72 kg, respectively. Statistically significant improvement in all subjective measures was observed after WakeUp was consumed in the morning (vigilance, ability to focus, and effectiveness

at work), as well as an improvement in the objective DSST. Drinking WakeUp in the morning resulted in a trend (albeit not statistically significant) improvement in iWRT. After consuming WakeUp in the evening, the only significant improvement was in DSST WakeUp, but there was a trend of improvement in iWRT and in subjective measures of vigilance, ability to focus, and effectiveness at work. Similar to previous studies, results consistently show that drinking WakeUp is associated with a 4-7% improvement in objective measures of alertness, with 6-22% improvement in subjective measures.

## BACKGROUND

Daytime somnolence is a very common phenomenon, affecting all ages and both genders. It may occur occasionally, commonly, or even chronically, due to a variety of etiologies. It may result in consequences such as road or work accidents, reduced function, diminished creativity and productivity at work, and increased health care utilization. Treatment of daytime somnolence may consist of changes in lifestyle, improving quality of nocturnal sleep, increasing the duration of nocturnal sleep, drinking wake promoting beverages or stimulant medications. Drinking coffee may improve vigilance and function by blocking adenosine receptors and by inhibiting phospho-di-esterase (PDE) which results in increased cAMP and adrenergic activity (CITATION). However, caffeine has a relatively short half-life and potential side effects, such as increased pulse rate and blood pressure. Moreover, regular coffee drinking results in tolerance and

substantial reduction of the wake promoting effects (CITATION).

The recently developed beverage WakeUp is a wake promoting beverage based on herbal ingredients consisting of Ginkgo biloba, Guarana, Elderberry extracts and Carobs sweetener. Guarana (*Paullinia cupana*) seeds have a long history of usage as a stimulant by Amazonian tribes (CITATION). It has been previously shown that Guarana improves memory performance and mood, and increases alertness, even in relatively low doses (CITATION). Ginkgo biloba is a unique tree which is native to China. Ginkgo biloba extracts are believed to have some important healing properties and are used in herbal medicine for asthma, bronchitis, fatigue, and tinnitus (CITATION). In addition to vigilance promoting, it has been shown to have favorable effects on memory (CITATION). It is currently used predominantly in Asia as a preventive treatment for Alzheimer's disease and other types of dementia (CITATION). Elderberry extract may improve the immune function (CITATION). Carobs sweetener primarily adds flavor to WakeUp, although its glucose content may also improve alertness.

Previous studies have shown that consuming WakeUp following lunch provided a substantial improvement in alertness and function. This was initially shown as a single dose effect in a double-blind study compared to caffeine and placebo (CITATION). In a later study, the same effects were observed after 30 days of usage (once daily after lunch). In studies so far, volunteers have drunk only one bottle of the beverage (100 ml) per day, in which case tolerance was not observed.

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## AIM

The purpose of the current study was to examine whether WakeUp beverage improves vigilance and performance subjectively and objectively when drunk twice in the same day: one in the morning and one in the afternoon/evening. We expected that improvements similar to those observed after lunch will be observed at different times of the day as well.

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## METHODS

The study was approved by the institutional review board (IRB, Helsinki committee) of Rambam Medical Center and all participants signed an informed consent prior to participation. Fifteen healthy volunteers (8 females) were studied twice in the same day: once in the morning and once in the evening. During each visit (morning and evening) they underwent a battery of tests prior to and 30 minutes after drinking 1 bottle (100 ml) of WakeUp. The battery of tests included measurements of vital signs, blood pressure, and validated, commonly used standard function and vigilance tests such as an immediate word recall test (iWRT, short term memory), digit symbol substitution test (DSST, concentration), and subjective rating (on a visual analogue scale - VAS) of their vigilance, ability to focus, and effectiveness at work. The results before drinking the beverage (baseline) were compared to the results 30 minutes after drinking, using a t-test. Results with  $p < 0.05$  were considered statistically significant.

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## RESULTS

The mean age of the participants was  $39 \pm 10$  years (range 24-56 years). They were all non-obese with an average height and weight of 169 cm and 72 kg, respectively. The various measures of their tests prior to and following WakeUp, in the morning and in the evening, are presented in the two tables below. In the morning, a statistically significant improvement in all subjective measures (vigilance, ability to focus, and effectiveness at work), and in the objective DSST was observed after drinking WakeUp. Drinking WakeUp in the morning resulted in a trend (albeit not statistically significant) improvement in iWRT. After consuming WakeUp in the evening, the only significant improvement was in DSST WakeUp, but there was a trend of improvement in iWRT and in subjective measures of vigilance, ability to focus, and effectiveness at work. Similar to previous studies, results consistently show that drinking WakeUp is associated with a 4-7% improvement in objective measures of alertness, with 6-22% improvement in subjective measures.

### Morning tests (on the average 08:38±00:58)

Test	Before drink	30 min after drink	P	Change (%) from BL after 30min
Pulse	77±9	77±10	NS	1
Systolic BP	115±16	116±17	NS	1
Diastolic BP	76±10	74±10	NS	-2.5
iWRT, correct	9.5±2.6	9.9±3.1	NS	4.2
DSST	84±17	91±18	0.001	8.7
Vigilance	6.5±2.3	7.5±1.8	0.03	15
Focusing	6.4±2.1	7.8±1.6	0.001	22
Effectiveness	7.4±1.8	8.2±1.6	0.013	11

### Evening tests (on the average 18:34±01:34)

Test	Before drink	30 min after drink	P	Change (%) from BL after 30min
Pulse	81±10	80±11	NS	-0.6
Systolic BP	119±19	122±21	NS	1.8
Diastolic BP	75±12	75±11	NS	-0.1
iWRT, correct	8.0±3.5	9.1±3.9	0.06	13
DSST	86±17	92±17	0.001	6.6
Vigilance	6.8±1.4	7.5±1.7	NS	11
Focusing	6.5±1.7	7.5±1.6	0.07	16
Effectiveness	7.4±1.5	7.8±1.6	NS	6

## DISCUSSION

The current study shows there is a substantial wake-promoting effect when consuming one serving of WakeUp beverage both in the morning and the evening WakeUp, with improvement in both objective performance and subjective perception of alertness. The magnitude of improvement following drinking WakeUp in the morning ranged from 4-9% in objective measures, and 11-22% in subjective, while the evening improvement ranged between 7-13% in objective measures, and 6-16% in subjective. The variability of performance was higher in the evening and thus some of the measures resulted in trend of improvement, without statistical significance. Nevertheless, in several different studies we have consistently observed around 10% improvement in alertness and performance after drinking WakeUp. The current study showed that drinking WakeUp during morning and evening hours has a similar effect to drinking it after lunch and it can repeatedly provide improvements when drunk twice in the same day. In accordance with previous studies, there were no adverse effects observed when drinking WakeUp during this study. Hemodynamic measures (heart rate and blood pressure) were not affected by WakeUp in the morning or the evening. Thus, as was observed in previous studies, WakeUp results in improved alertness without adverse hemodynamic effects.

The major limitation of the current study is the relatively small sample size of 15 participants, all healthy. This probably explains the lack of statistical significance in some measures. Nevertheless, there is an ongoing trend demonstrating the wake-promoting effects of this herb-based beverage. These effects seem to not be dependent on the time of drinking and are not limited to only one bottle per day.

**Fig1:** % of change morning / evening - before WakeUp vs. 30min after WakeUp

