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Effects of kratom on driving: Results from a cross-sectional survey, ecological momentary assessment, and pilot simulated driving Study

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ABSTRACT

Objectives: Despite widespread kratom use, there is a lack of knowledge regarding its effects on driving. We evaluated the self-reported driving behaviors of kratom consumers and assessed their simulated-driving performance after self-administering kratom products.

Methods: We present results from: 1) a remote, national study of US adults who regularly use kratom, and 2) an in-person substudy from which we re-recruited participants. In the national study (*N*=357), participants completed a detailed survey and a 15-day ecological momentary assessment (EMA) that monitored naturalistic kratom use. For the remote study, outcomes were self-reported general and risky driving behaviors, perceived impairment, and driving confidence following kratom administration. For the in-person substudy, 10 adults consumed their typical kratom products and their driving performance on a high-fidelity driving simulator pre- and post-kratom administration was evaluated. **Results:** Over 90% of participants surveyed self-reported driving under the influence of kratom. Most reported low rates of risky driving behavior and expressed high confidence in their driving ability after taking kratom. This was consistent with EMA findings: participants reported feeling confident in their driving ability and perceived little impairment within 15-180 min after using kratom. In the in-person substudy, there were no significant changes in simulated driving performance after taking kratom.

Conclusions: Using kratom before driving appears routine, however, self-reported and simulated driving findings suggest kratom effects at self-selected doses among regular kratom consumers do not produce significant changes in subjective and objective measures of driving impairment. Research is needed to objectively characterize kratom's impact on driving in regular and infrequent consumers.

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Kratom; driving simulator; cross-sectional survey; ecological momentary assessment

Introduction

Kratom products, derived from the plant *Mitragyna speciosa*, are consumed as powders, teas, and concentrated extracts, and sometimes smoked. In the United States (US), people report using kratom to improve energy, focus, and mood, and to address symptoms of anxiety, depression, pain, fatigue, and substance use disorders (SUDs) (Grundmann et al. 2023; Smith & Lawson 2017; Smith, Dunn, Rogers, Garcia-Romeu, et al. 2022). Kratom is legal in most states, but some states have adopted versions of the Kratom Consumer Protection Act, which regulates sale and use of kratom products and encourages Good Manufacturing

Practice among vendors. The regulatory status of kratom in the US, and the public-health implications of its use or prohibition, are still being determined (Henningfield et al. 2022).

Many who use kratom do so regularly over long periods, more than once daily (Garcia-Romeu et al. 2020; Smith et al. 2021; Smith, Rogers, et al. 2022). There is still a lack of scientific data on effects of commercially available kratom products; efforts are complicated by sheer number bioactive alkaloids in kratom (Berthold et al. 2022; Hiranita et al. 2022; Obeng et al. 2019, 2022). The combination of widespread use and uncharacterized, sometimes intoxicating effects raises important public-health questions.

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The question addressed in this study is whether acute exposure to kratom, in regular consumers, affects driving behavior. There are only limited data on driving habits and behaviors in kratom consumers. A survey in Thailand found that only a small number of active drivers reported using kratom before driving (Ingsathit et al. 2009). A case report in the US described an instance of impaired driving after kratom exposure, but the results were complicated by the driver's use of amphetamine and citalogram and the timing of field sobriety tests (Wright 2018). Another case report identified the kratom alkaloid mitragynine and its active metabolite 7-hydroxymitragynine, along with the synthetic cathinone a-pyrrolidinovalerophenone (a-PVP), in the blood of a driver suspected of drug-impaired driving (Knoy et al. 2014). These reports are difficult to interpret due to unknown kratom doses and co-use of other substances. There are no controlled experimental studies of the extent to which kratom influences driving performance.

Our exploratory study aimed to first evaluate the self-reported driving behaviors of people who regularly use kratom, rather than occasional users, and to determine whether responses differed based on their reported frequency of kratom use. Second, we aimed to assess driving performance following kratom product self-administration in a controlled setting among some of those participants. Thus, this paper reports relevant results from 2 studies: (1) a national cross-sectional survey with 15-day ecological momentary assessment (EMA) to measure self-reported perceived impairment and driving confidence accompanying regular kratom use, and (2) a laboratory-simulated driving performance study following acute morning kratom selfadministration after overnight abstinence. We did not make a priori hypotheses about how participants would perform on the driving outcomes, because, based on existing literature, we anticipated several possible outcomes: performance could improve after kratom due to a normalizing effect reflecting physical dependence, or performance could be impaired due to acute effects of kratom that occur even in tolerant consumers (Smith, Dunn, Rogers, Garcia-Romeu, et al. 2022; Smith, Feldman, Dunn, McCurdy, Weiss, et al. 2023; Smith et al. 2024).

Methods

Sample and recruiting strategy

Between July and October 2022, US adult participants were enrolled into a three-phase study: a two-phase fully remote study (for detailed methods, see Smith, Feldman, Dunn, McCurdy, Grundmann, et al. 2023; Smith, Rogers, et al. 2023) and an in-person laboratory study (NCT05457803). Candidates were recruited using social media, kratom advocacy and vendor groups, podcasts, public flyers in Baltimore and surrounding areas, and word of mouth. For Study 1, participants completed a detailed online cross-sectional survey (n=395) and 15-day period of EMA (n=357 completers) via a smartphone app. To be eligible for Study 1, candidates had to report using kratom regularly (≥ 3 times weekly for ≥ 4 consecutive weeks), reside in the US, own a smartphone, be willing to complete all study activities, pass an informed-consent quiz ($\geq 80\%$ correct), and demonstrate

English language proficiency (verified by open-text screening questions). Exclusion criteria were: missing ≥1 data validity check on our screener, screening on a device that could not be verified as located in the US, inability to adhere to study tasks (by failing the informed-consent quiz), or being incarcerated. Infrequent consumers were excluded as this study sought to obtain momentary data; the inclusion of infrequent kratom consumers into an EMA study on kratom would not permit use patterns to be determined.

Study 2 identified ten adults who had completed Study 1; they were invited to participate in a laboratory study within the National Institute on Drug Abuse Intramural Research Program on the Johns Hopkins Bayview Medical Campus in Baltimore, MD. To be eligible for Study 2, participants had to be 18 years of age or older (no upper age limit), have completed Study 1, live within 150 miles of the clinic, and report using kratom products ≥3 times weekly for ≥4 consecutive weeks prior to study enrollment. Participants were ineligible for Study 2 if they were pregnant or nursing, or if they reported a history of vertigo or being prone to motion sickness, which could interfere with the driving-simulation test.

For both studies, participants were not excluded if they reported other substance use (e.g., over-the-counter medications, illicit substances, supplements). All participants provided voluntary informed consent for both studies and both studies were approved by the National Institutes of Health Institutional Review Board (NCT05457803).

Study 1. Kratom cross-sectional survey and ecological momentary assessment

Screening, enrollment, and compensation

Eligible candidates were emailed an enrollment link that expired after 9 days, during which they were to read the consent document, ask the study team questions, and complete the consent quiz. After consent, candidates were required to attest electronically that they were over 18, resided in the US, and were voluntarily consenting to participate. Participants were compensated \$27.50 for completing the cross-sectional survey and \$7.50 for each day of full adherence to EMA.

Survey and EMA driving behaviors and driving-confidence assessments

Within this same 9-day period, enrolled participants were asked to complete a survey on demographic and health information and on their current and prior kratom and other substance use. The full survey instrument is available on request.

In this report, we focus on questions related to driving. We assessed participants' experiences with five specifically developed pilot questions about kratom use and driving, and one open-ended text response. We then administered the Driving Habits Questionnaire (DHQ) (Owsley et al. 1999), which assesses driving behaviors (e.g., driving 10 mph or more over the speed limit) and driving history and habits

(e.g., "how long have you been driving?", "how often do you drive?"), including items related to driving under the influence of substances (e.g., alcohol, cannabis). Participants rated each item on using a Likert scale ranging from "Never" to "Always."

During the EMA phase, participants were asked to report each time they used kratom along with circumstances surrounding use. Each event-contingent use entry consisted of 10 items. Use could also be reported as part of a randomized prompt issued during waking hours (twice per day) and in an End-of-Day diary, where they could report any kratom doses taken that day and not already reported. Use events reported during the End-of-Day diary were designated into appropriate time bins over the 24-h period. All reported use events were compiled for each participant into 24 one-hour bins, based on self-reported sleep-wake pattern hours, beginning with the expected wake time for each day (see Data Analysis below).

Within 15-180 min after an event-contingent kratom-use entry, participants were randomly prompted (up to twice a day) to complete a short set of follow-up questions (the prompt expired after 30 min). This follow-up prompt asked two questions related to impairment and driving. First, "How impaired do you feel as a result of the kratom?" with responses on a visual analogue scale (VAS) slider, with 0 meaning "Not at all impaired" and 100 meaning "Unable to function." Second, "Based on how you feel from your last kratom use, how confident would you be driving a vehicle right now?" with responses on a similar VAS slider (0 meaning "Extremely unconfident" and 100 meaning "Extremely confident").

Study 2. In-person kratom product self-administration and simulated driving phase

Participants in Study 2 were scheduled to complete two visits. The first visit comprised informed consent and an acclimation drive on the driving simulator (described below). The acclimation drive was a driving scenario distinct from the two test drives (described below) that was designed to expose the participants to the various tasks in order to minimize practice and anticipatory effects on study outcomes. On the first day, participants also provided three samples of the kratom product they were regularly using, with each sample reflective of participants' current typical kratom dose (e.g., 3 capsules, 2 grams; see Supplemental Table 1). Samples were obtained by the study nurse and taken to our Pharmacy for examination, weighing, and secure storage. The second visit comprised an approximately 8-h long session. Participants were asked to refrain from using kratom the morning of their session until after arriving at our clinic; use after midnight (before sleeping) was discouraged but not prohibited. As the substudy sought to model naturalistic kratom use, we attempted to limit manipulations; participants could medications or supplements that were part of their daily routines, except substances with known intoxicating effects (e.g., cannabis). Prohibiting the use of all substances that participants consumed as part of their daily routine

could have complicated interpretation of the results. Upon participant arrival, nurses conducted a urine drug screen, breathalyzer, and survey of all medications or supplements used during the past 24h. All participants self-reported that their time of last kratom use was at least 10h prior to their session dosing time. Participants then completed assessments of subjective drug-effect ratings, cognitive and psychomotor function, and cardiovascular effects at baseline and post-kratom administration. Findings unrelated to driving and relevant subjective drug ratings are reported elsewhere, along with other participant details (e.g., urine drug test results, medication timepoints; Smith et al. 2024)

Prior to their baseline driving simulation, participants completed the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al. 1989), which assesses sleep patterns and sleep disturbances in the past month, and the Karolinska Sleepiness Scale (KSS), which assesses level of sleepiness from 1 (extremely alert) to 9 (very sleepy, great effort to keep awake, fighting sleep). Participants completed a short practice drive to reacclimate them to the driving simulator (10 min), then immediately completed their baseline simulated drive (15 min).

Following the baseline simulated drive, the nurse gave participants one of the three kratom doses that they had provided during their first visit and reserved another dose for analysis; unused doses were given back to participants at the end of the session. A nurse observed the participant orally self-administering their regular kratom product dose in the manner they typically consumed it (e.g., capsule, raw powder, or pulverized plant matter dissolved in water). Baseline measures were then repeated, and alertness was assessed for the second and final time before the post-dose driving simulation. The average time between kratom administration and starting the second simulated drive was 82.2 min (SD= 20.8; Range = 55-129). Maximum plasma concentrations (C_{max}) of mitragynine in humans are expected between 0.75-1.50h after oral administration (Tanna et al. 2022), suggesting that the post-kratom administration drive was assessed during the active window.

Driving performance and outcomes

Detailed descriptions of driving simulations are in Zamarripa et al. (2022). Details on the STISIM M4000-R Drive simulator details are in the online Supplementary Appendix. Briefly, participants completed two 15-minute driving simulations pre- and post-kratom administration. Simulations consisted of routine driving through city and rural segments across 13.3 miles (21.4 kilometers) and participants were encouraged to drive as they normally would, including when they encountered traffic lights, stop signs, and other cars on the road. Speed-limit signs were posted in the simulations. Drives yielded the following general outcomes: Accidents (number of collisions, pedestrians hit, and off-road accidents), Rule-Following (number of missed stop signs, stops at red lights, and illegal turns), Speed (number of speed exceedances, total drive length, and percentage of time driven over the speed limit), and Lateral Movement (number of centerline crossings, road edge excursions, and percentage of time driven out of lane). Four controlled driving tasks were also programmed into the routine drives: a car-following task, a divided attention task, a crash avoidance, and a stop-light reaction test. The two drives differed only in the presentation of stimuli in the tasks and placement of the stoplight interaction (see below). The order of driving segments was kept consistent across the two drives though the order with which the two drives were completed was counterbalanced across participants.

During the first 8 min of the drives, participants completed a car-following task and divided attention task; no other cars or driving obstacles were present during these two tasks. During the car-following task, participants were instructed to follow a lead vehicle at a constant distance while the lead vehicle's speed fluctuated between 50 and 70 mph in a sinusoidal manner. The primary outcomes for the car-following task were standard deviation of lateral position (SDLP; an index of lane weaving), and coherence score, which reflects how well the participant's overall data matched that of the lead vehicle. Coherence is expressed as a correlation from 0-1, where 0 indicates no correlation between the participant's and lead vehicle's data, and 1 indicates perfect correlation between the two vehicles. During the divided attention task, participants were instructed to maintain a speed of 55 mph, to maintain their lane position, and to respond to symbols that appeared in one of the four designated quadrants on the left or right monitor. There was a total of 20 symbols presented, and participants had a maximum of 5s to respond. The primary outcome measures for the divided attention task were SDLP, the standard deviation of speed (SDSP), and the mean reaction time to respond to the ancillary symbols.

During routine driving segments, which encompassed the final 7 of the 15 min, two specific tasks of interest occurred: a crash avoidance and a stoplight reaction test. For the crash avoidance, participants responded to an unexpected event (e.g., a pedestrian walking across the road). The avoidance was initiated based on the driver's distance from the event (specifically, when their headway time was 2.5 s from the object). The avoidance location differed in each drive (both avoidances were children but their placement in the drive differed) to minimize practice effects. The primary outcome of the crash avoidance was the reaction time to elicit a response (either gas or brake). The stoplight reaction test required participants to respond to a traffic light that changes from green to yellow to red. The light was programmed to change from green to yellow when the driver was 5.5 s away and the yellow light lasted exactly 3.5 s. The primary outcome for this test was the reaction time to elicit a response after the light turned yellow (either gas or brake). The reaction times for both the crash avoidance and stoplight reaction test were determined by measuring the exact response time (in seconds) that the pedal response was initiated following the initial presentation of the relevant stimulus (i.e., the brake response time was measured following the initiation of avoidance, while the gas/brake response time was measured after the presentation of the yellow light).

For self-reported driving confidence, participants also completed the following series of self-reported VAS ratings pre- and post-driving to assess their perceived confidence to drive using the following two questions: "What is your confidence to drive?", and "Would you feel comfortable to drive right now?". These results can be found in the Appendix.

Kratom product

Each participant provided a typical dose of their preferred kratom product. Samples were shipped to the University of Florida Translational Drug Development Core where 10 kratom products were quantified for eleven major and minor alkaloids (Kamble et al. 2021; Sharma et al. 2019). The average composition of alkaloids of the kratom products can be found in the Appendix. The dose range between kratom products was 1.1-10.9g.

Data analysis

Study 1 outcomes were assessed by first categorizing participants into clusters based upon kratom use frequency as reported during EMA and then examining outcomes as a function of cluster assignment to model a "dose-dependent" effect of kratom on self-reported driving. Cluster analysis was based upon the mean number of uses in each of the participant's time bins, which was conducted using finite-mixture modeling (FlexMix package in R; Leisch 2004). This modeling approach simultaneously incorporated two independent partitions of the uses per hour data that were normalized both within and between participants (i.e., pattern of use in each hour relative to the participant's own level of use, and relative to other participants). Five clusters were identified as optimal (labeled A though E). The number of clusters was chosen based on the Bayesian Information Criterion, to avoid underfitting or overfitting. Therefore, Cluster A reported the highest frequency of use and Cluster E reported the lowest. All data were analyzed to determine normality. Cross-sectional data from Study 1 were then analyzed using parametric tests with normal distributions. One-way analysis of variance (ANOVA) with Tukey's comparisons was employed to compare Dosing Cluster (Clusters A, B, C, D, E) as a between-subject variable for participant demographics and responses on the cross-sectional Likert scale responses on the driving history questionnaire. Nonparametric tests were employed for data with non-normal distributions, specifically Kruskal-Wallis evaluations of differences between the five clusters, followed by Dunn's multiple comparisons tests to compare specific clusters. Study 1 analyses for the cross-sectional data were conducted using GraphPad Prism version 9.4.1 and the threshold for statistical significance was set at a p value of 0.05 for all tests. For the EMA data, results were analyzed using Bayesian ordered beta regression (Kubinec 2022); these results are reported and plotted as medians with Bayesian 90% credible intervals, and paired comparisons are based on highest density intervals calculated using the "emmeans" R package (Lenth 2021). Study 1 EMA analyses were conducted using the "ggplot2" package in R (Wickham 2016).

Study 2 analyses consisted of paired-samples t-tests to compare all driving outcomes between the pre- and post-kratom administration simulated drives from Study 2 and Spearman's correlations to evaluate quantitative blood kratom alkaloid concentrations and change-from-baseline measures of SDLP, SDSP, and reaction time from the individual tasks in the driving simulation. These measures were chosen because they demonstrate good sensitivity to drug-impaired driving (Arkell et al. 2020; Freydier et al. 2014; Miller et al. 2020). Finally, VAS scores on the subjective driving questionnaires were analyzed using a one-way repeated measure ANOVA with the within-subject factor of Time (0-2.75h). Dunnett's multiple comparisons were used to compare all timepoints to baseline (i.e., Timepoint 0). Study 2 analyses were conducted using GraphPad Prism version 9.4.1 and the threshold for statistical significance was set at a p value of 0.05 for all tests.

Results

Cross-sectional survey and ecological momentary assessment on driving behaviors

Study 1 Outcomes

Survey participant demographics. A total of 1,152 eligible candidates were emailed an invitation to consent, of which 395 (34.2%) consented, enrolled, and completed the crosssectional survey. Participants (N=38) were excluded if they did not complete the EMA phase because they could not be included in the cluster analysis. Participants from the

cross-sectional survey were divided into five unique clusters that corresponded to their typical daily frequencies and patterns of kratom use across the EMA phase (described above). Among these clusters, only those who endorsed that they drive were included in these analyses. A total of 48 participants were excluded because they endorsed not driving. The final sample size for Clusters A, B, C, D, and E were 39, 60, 65, 72, and 73, respectively. Across all groups, clusters did not differ in self-reported gender, ethnicity/race, education or employment (Table 1). All clusters were predominately white, ranging from 78.3%-89.2% of the clusters' makeup. Groups did not differ in age of first kratom use or past 30-day use of caffeine, nicotine/ tobacco, alcohol, or cannabis products. There was a main effect of age (F [4,303] = 4.204; p = .0025), and past 30-day kratom use (F [4,303] = 20.09; p < .0001) observed between the five clusters (p's < .05). Specifically, participants in Cluster A, which had the highest daily kratom intake, were older than the participants in Clusters D and E, which had the lowest. Further, Cluster E had reduced kratom use over the last 30-days relative to all other groups (p's < 0.05). Additional Study 1 outcomes are reported elsewhere (Smith et al. 2024).

Self-reported driving patterns across people who use kratom. Driving patterns across clusters can be found in Table 2. In each cluster, a vast majority (i.e., ≥ 89%) of the participants had their driver's license. Clusters did not differ in their average number of driving miles per week, number of lifetime traffic tickets, or number of lifetime car accidents. Similar to the general demographics, there was a main effect

Table 1. Survey participant demographics.

| | _ | Use-frequency Cluster | | | | | | |
|--|--------------------------------|-----------------------|-------------------------|-------------------------|--------------------------|--------------------------|--|--|
| Demographic | | A (N=39) | B $(N = 60)$ | C (N=65) | D $(N = 72)$ | E (N=73) | | |
| Age (in years) | Mean (SD) | 44.2 (12.6) | 37.6 (9.7) | 39.2 (10.9) | 36.6 (10.3) ^a | 36.0 (11.2) ^a | | |
| | Range | 28-69 | 18-76 | 19-66 | 21-71 | 19-69 | | |
| Gender | Male | 20 (51.3%) | 29 (48.3%) | 41 (63.1%) | 40 (55.6%) | 45 (61.6%) | | |
| [n, (%)] | Female | 18 (46.2%) | 30 (60.0%) | 22 (33.9%) | 30 (41.7%) | 26 (35.6%) | | |
| | Other | 1 (2.6%) | 1 (1.7%) | 2 (3.1%) | 2 (2.8%) | 2 (2.7%) | | |
| Ethnicity [n, (%)] | Hispanic/Latinx/Spanish Origin | 2 (5.1%) | 4 (6.7%) | 5 (7.7%) | 2 (2.8%) | 6 (8.2%) | | |
| , | NOT Hispanic/Latinx/Spanish | 37 (94.9%) | 56 (93.3%) | 60 (92.3%) | 70 (97.2%) | 67 (91.8%) | | |
| Race [n, (%)] | American Indian/Alaska Native | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 1 (1.4%) | | |
| | Asian | 1 (2.6%) | 0 (0%) | 1 (1.5%) | 0 (0%) | 0 (0%) | | |
| | Black/African American | 0 (0%) | 0 (0%) | 0 (0%) | 1 (1.4%) | 2 (2.7%) | | |
| | White/Caucasian | 33 (84.6%) | 47 (78.3%) | 58 (89.2%) | 61 (84.7%) | 62 (84.9%) | | |
| | More than one race | 5 (12.8%) | 13 (21.7%) | 6 (9.2%) | 8 (11.1%) | 7 (9.6%) | | |
| | Self-described | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 1 (1.4%) | | |
| Education (at least some college) | n, % | 33 (84.6%) | 49 (81.7%) | 57 (87.7%) | 57 (79.2%) | 63 (86.3%) | | |
| Past 12 months employment (at least part-time) | n, % | 28 (71.8%) | 45 (75.0% | 50 (76.9%) | 51 (70.8%) | 53 (72.6%) | | |
| Age of First Kratom Use | Mean (SD) | 36.9 (12.1) | 32.5 (9.8) | 34.2 (11.4) | 31.4 (10.4) | 30.8 (11.1) | | |
| Past 30-Day Product Use | | | | | | | | |
| Past 30-Day Kratom Use | Number of days [Mean (SD)] | 29.8 (1.3)b | 29.4 (1.9) ^b | 29.1 (2.1) ^b | 28.3 (2.8)b | 24.7 (6.6) | | |
| Past 30-Day Caffeine Use | Number of days [Mean (SD)] | 25.9 (8.6) | 23.6 (10.9) | 27.0 (7.6) | 22.3 (10.8) | 23.6 (9.9) | | |
| Past 30-Day Nicotine/ Tobacco Use | Number of days [Mean (SD)] | 8.4 (13.6) | 5.2 (11.2) | 6.9 (12.2) | 6.8 (12.2) | 4.0 (9.5) | | |
| Past 30-Day Alcohol Use | Number of days [Mean (SD)] | 2.9 (6.3) | 2.4 (5.2) | 4.4 (7.5) | 4.3 (7.7) | 6.0 (8.4) | | |
| Past 30-Day Cannabis Product Use | Number of days [Mean (SD)] | 6.6 (10.7) | 9.3 (13.9) | 9.3 (12.9) | 8.0 (11.8) | 7.8 (11.7) | | |

Note. SD: Standard Deviation; n: sample size; %: percentage.

aindicates a significant difference from Cluster A (p < 0.05).

bindicates a significant difference from Cluster E (p < 0.05). Clustering was based on timing and frequency of kratom use over 15 days of ecological momentary assessment; Cluster A had the highest frequency of use and Cluster E had the lowest.

of years driving (F [4, 304] = 3.689; p = .006), where Clusters D and E had less years driving relative to Cluster A. Table 2 indicates that the self-reported rates of driving under the influence of kratom were similar across all clusters, with over 85% of participants in each group acknowledging doing so. Furthermore, a majority (i.e., >90%) of the participants in each cluster reported routinely driving under the influence of kratom. Finally, there were no differences between clusters in reported having ever driven under the influence of alcohol or cannabis. However, there was a main effect of past-year driving under the influence of alcohol (p = .0086), where Cluster E had higher self-reported days of driving under the influence of alcohol relative to Clusters A and B.

The driving history questionnaire outcomes between the five clusters are shown in Figure 1. Across all of the driving questionnaire outcomes, there were no significant differences across any of the main outcomes. Most participants, regardless of cluster, reported "Rarely" or "Never" engaging in dangerous driving behaviors. Additionally, when asked about their confidence to drive under the influence of kratom, most participants reported a high degree of confidence (i.e., > 95 VAS Score) in their driving ability while under the influence of kratom (Table 2).

Consistent with this data, participants' confidence to drive and perceived level of impairment reported during the EMA phase are shown in Supplemental Figures A1. Regardless of clusters, all participants reported a high degree of confidence in their perceived driving ability when prompted to score their confidence to drive following kratom administration. Similarly, participants reported low perceived levels of impairment following kratom administration.

Study 2 outcomes

Participant demographics

Characteristics of the participants who completed the in-person laboratory study (N=10) are shown in Supplemental Table A1. Participants were predominantly non-Hispanic white (n=9), with one individual endorsing more than one race (i.e., Asian/white). Their mean (SD) age was 41 years old (10.3). On average, participants had regularly used kratom (without a break) for 3.5 years (SD = 2.6 years; range: 0.58-8 years) prior to their first session. The average amount of kratom self-administered across participants during the in-person session was 5.1g (SD = 2.8g; range: 1.1-10.9g). No participants experienced unanticipated or serious adverse events during the study. There was no change in KSS score following kratom administration, indicating that levels of alertness before and after kratom administration did not significantly differ (p = .34). Following kratom administration, all participants reported an increase in subjective drug ratings of "feel drug effect" relative to baseline that peaked at the 1.25 hr timepoint.

Simulated driving outcomes

General outcomes. Overall, baseline values did not differ relative to post-kratom administration values on any variables collected across the four general driving categories (i.e., Accidents, Rule-Following, Speed, or Lateral Movement). Overall, there were no instances of pedestrians hit, collisions, off-road accidents, or illegal turns. Participants also demonstrated good adherence to rules, with few missed stop signs (mean percentage [SD] 10% [21.1] pre and 0 post) and good adherence to red lights (mean percentage of stops at red lights [SD] 90.0% [31.6] pre and 90.0% [31.6] post). Similarly, participants maintained consistent throughout the drives, with no changes in speed exceedances, total run length, and percentage of driving over the speed limit. Finally, participants demonstrated similar lane positioning performance, with the number of centerline crossings and road edge excursions, and the percentage of driving outside of the line not differing between the preand post-kratom administration drives.

Task-based outcomes. Figure 1 describes the changes in SDLP and coherence scores on the car-following task before

Table 2. Self-reported driving patterns of people who use kratom.

| | | Use-frequency Cluster | | | | | |
|---|-----------|-----------------------|------------------------|---------------|--------------------------|--------------------------|--|
| Driving Characteristics | | A (N=39) | B (N=60) | C (N=65) | D (N=72) | E (N=73) | |
| Have License | n, % | 35 (89.7%) | 59 (98.3%) | 64 (98.5%) | 71 (98.6%) | 68 (93.2%) | |
| Years Driving | Mean (SD) | 26.9 (12.6) | 21.0 (10.0) | 22.8 (12.6) | 19.2 (11.0) ^a | 19.2 (12.3) ^a | |
| Average Driving Miles Per Week | Mean (SD) | 152.0 (162.0) | 144.2 (189.7) | 182.0 (190.8) | 138.9 (162.0) | 132.3 (138.9) | |
| Lifetime Number of Driving Tickets | Mean (SD) | 2.2 (1.7) | 2.6 (3.2) | 2.3 (2.2) | 1.6 (1.5) | 1.9 (2.8) | |
| Lifetime Number of Car Accidents | Mean (SD) | 1.5 (1.6) | 1.2 (1.2) | 1.5 (1.6) | 1.3 (1.5) | 1.4 (1.8) | |
| Ever driving under the influence of Kratom | n, % | 36 (92.3%) | 59 (98.3%) | 61 (93.9%) | 65 (90.3%) | 63 (86.3%) | |
| Confidence to drive under the influence of kratom (0-100) | Mean (SD) | 97.9 (7.1) | 98.5 (4.4) | 96.8 (8.9) | 96.8 (9.7) | 98.0 (8.1) | |
| Ever driving under the influence of alcohol | n, % | 22 (56.4%) | 35 (58.3%) | 35 (53.9%) | 32 (44.4%) | 40 (54.8%) | |
| Past year driving under the influence of alcohol (Days) | Mean (SD) | 0 (0) ^b | 0.1 (0.5) ^b | 0.8 (2.1) | 1.5 (7.1) | 3.4 (9.9) | |
| Ever driving under the influence of cannabis | n, % | 10 (25.6%) | 16 (26.7%) | 21 (32.3%) | 15 (20.8%) | 14 (19.2%) | |
| Past year driving under the influence of cannabis (Days) | Mean (SD) | 24.7 (78.7) | 27.6 (78.1) | 62.8 (127.8) | 50.1 (107.7) | 32.3 (84.4) | |

Note. SD: Standard Deviation; n: sample size; %: percentage.

aindicates a significant difference from Cluster A (p < 0.05).

bindicates a significant difference from Cluster E (p < 0.05).

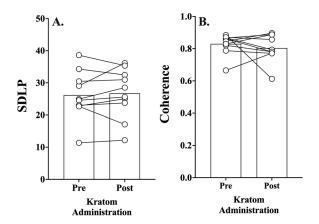


Figure 1. Study 2: Mean simulated driving performance for (A) the standard deviation of lateral position (SDLP), and (B) coherence score on the car-following task before and after kratom administration. Lines and symbols illustrate changes between participants pre- and post-drive performance. Higher SDLP and lower coherence values indicate poorer driving performance.

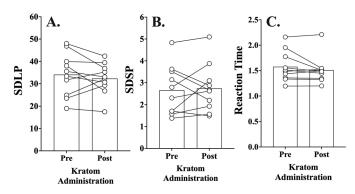


Figure 2. Study 2: Mean simulated driving performance for (A) the standard deviation of lateral position (SDLP), (B) the standard deviation of speed (SDSP), and (C) reaction time on the divided attention task before and after kratom administration. Lines and symbols illustrate changes between participants preand post-drive performance. Higher values for the three outcomes indicate poorer driving performance.

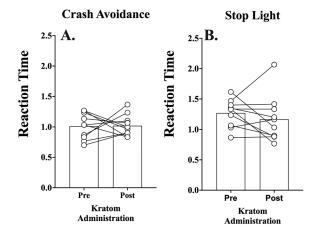


Figure 3. Study 2: Mean reaction times during simulated driving performance at the (A) crash avoidance, and (B) red traffic light before and after kratom administration. Lines and symbols illustrate changes between participants preand post-drive performance. Higher reaction time values indicate poorer driving performance.

and after kratom self-administration. Following kratom selfadministration, there were no significant changes across the three main outcomes. Only one out of the ten total participants showed a modest increase in SDLP and a decrease in coherence score (both indicators of impaired driving performance); remaining participants all showed stable performance from pre to post-kratom selfadministration. Figure 2 illustrates the performance on the divided attention task before and after kratom selfadministration. Following self-administration of kratom, there were no overall changes in SDLP, SDSP, or mean reaction time (p's>0.05). Additionally, there were no observable trends (i.e., a constant decrease or improvement in performance) among participants across the three outcomes following drug administration.

Figure 3 shows the reaction time for the crash avoidance, and time to brake at the stop light stimulus before and after kratom self-administration. There were no changes in reaction time to the crash avoidance event following kratom self-administration. Similarly, reaction time to brake at the stop light did not differ between pre- and post-kratom self-administration drives (p's>0.05). Again, no observable trends among the participants' reaction times were present across the two reaction time-based outcomes.

Correlations between driving outcomes and kratom alkaloids

Although driving outcomes did not vary significantly as a function of kratom administration, blood plasma concentrations for kratom alkaloids were correlated with the change-from-baseline values for select driving outcomes to determine if trends emerged as a function of alkaloid concentrations. Corynoxine and corynoxine B were not detected in blood plasma and therefore could not be correlated to driving outcomes. Across all outcomes, SDLP from the car-following task was negatively correlated with blood plasma MTG, 7-HMG, and corynantheidine. However, there was no correlation between SDLP from the divided attention task and plasma MTG, 7-HMG, and corynantheidine. No significant correlations were observed across other driving outcomes.

Discussion

The present analyses conducted two studies aimed at evaluating driving habits and performance associated with kratom use among adults who use kratom regularly. In Study 1, participants completed a survey and intensive EMA study to characterize their driving habits and beliefs while using kratom. In Study 2, a subsample of participants from Study 1 completed a controlled laboratory study in which they self-administered their usual dose of kratom and completed a simulated driving assessment to examine the extent to which kratom impairs driving performance.

Understanding the driving behaviors and potential impairing effects of kratom across daily activities (e.g., driving), is important given the growing popularity of kratom products

and their use as a part of everyday life. Kratom usage shares similarities with caffeine consumption, as it is often taken to enhance productivity, focus, and energy, rather than for acute intoxication purposes like alcohol (Smith, Dunn, Rogers, Grundmann, et al. 2022). Our findings from the survey and EMA self-report indicate individuals who regularly use kratom do not generally perceive their kratom dose to be impairing and, consequently, may drive shortly after use. Consistent with participants' self-report, kratom administration in the laboratory, on average, did not impair simulated driving performance relative to baseline (prior to kratom use). Together, these findings suggest that the acute effects produced by commercially available kratom products, when taken at a self-selected "typical" dose, do not alter perceptions of driving ability, nor do they appear to impair driving function (on average) among adults who regularly use kratom.

Kratom is currently legal in 45 US states and its use is increasing rapidly, but our understanding of its effects, including its impact on driving behavior, lags behind (Babu et al. 2008; Grundmann 2017; Smith, Dunn, Rogers, Grundmann, et al. 2022; Smith, Feldman, Schriefer, et al. 2023; Swogger et al. 2015). To our knowledge, this study is the first to investigate the driving habits and behaviors of people who use kratom regularly. Findings from the cross-sectional survey suggest that frequent kratom users routinely drive under the influence of kratom (>90% of participants in each cluster) but endorse low-risk driving behaviors (e.g., endorse rarely speeding or tailgating). These findings did not differ based on kratom use dosing patterns. During the EMA phase, participants reported little-to-no impairment in their daily functioning and high confidence in their ability to drive. Compared to other commonly used substances such as alcohol and cannabis (Colonna et al. 2021; Kelley-Baker et al. 2017; Ronen et al. 2010), kratom users report fewer risky driving behaviors (such as driving over the speed limit) and less perceived impairment of driving function. However, both the cross-sectional and EMA phases of the study were based on self-report and were limited in their ability to measure driving-related behaviors after kratom intake.

We also examined simulated driving performance in a controlled lab setting following kratom self-administration in a small subset of participants (N=10). Our results indicate that overall, when persons who were kratom-experienced consumed their typical dose of kratom, they did not demonstrate any decrement in driving performance as measured across various outcomes (i.e., SDLP, SDSP, reaction time) that are known to be sensitive to drug- or alcohol-induced driving impairment (Brooks-Russell et al. 2021; Veldstra et al. 2015). That said, one participant (#3) did experience a general decrease in performance during the car-following task but not across any other outcomes. Further, we found negative association between driving performance and blood plasma concentrations of MTG, 7-HMG, and corynanthidine. However, these associations were not consistent across driving outcomes, or present for any other kratom alkaloid. Although we did not detect acute driving impairment following kratom administration, caution is still advised in the absence of larger, controlled trials. While psychomotor performance, which was also assessed at baseline, showed no indicators of impairment nor were obvious signs of impairment directly observed by the study team, it is possible that subtle impairment was present from either mild withdrawal symptoms (from participants having skipped their typical morning dose) or from the lingering effects of their last kratom dose. Because the last dose was approximately 10h before baseline, we do not suspect the latter (Smith, Rogers, et al. 2023). It may be that participants were under the influence of their last kratom dose insofar as their bodies were still metabolizing kratom alkaloids, but in the meaningful sense of the term 'under the influence' we do not have reason to believe that participants were under the influence of kratom acute effects from their last dose (Smith, Rogers, et al. 2022; Smith et al. 2024). Another point of caution is that higher doses of kratom may affect driving ability and any kratom dose among a kratom naïve individual could produce an impairing effect not observed here. Our subsample is, by design, not intended to reflect everyone who uses kratom and should be understood as comprising adults who use regularly and who may have some tolerance. Finally, drug-interactions between kratom and commonly used medications, illicit drugs, or supplements can occur. Given the multitude of factors that may influence the potential of kratom to be impairing, our initial findings are presented as a first step in a longer path of investigation.

Indeed, there are several limitations to the present study. Firstly, the study used a convenience sampling technique to capture the naturalistic behaviors of people who use kratom regularly. Thus, it is possible that the outcomes collected do not represent all individuals who use kratom, particularly people who consume kratom infrequently. More research is needed to extend this work to people who use kratom for recreation rather than routine. However, this study was an important stride toward understanding driving behaviors and impairment associated with the use of kratom regularly. Secondly, the laboratory study included a small population of people who use kratom regularly, which makes it difficult to generalize the findings to people who use kratom infrequently or who use in combination with other substances while driving. As all participants used some raw powder formulation, we cannot make inferences about other products, such as isolated extracts for specific kratom alkaloids.

Future studies will need to investigate the impairing or enhancing effects of kratom on driving performance across different groups, including individuals who infrequently use kratom and those who use kratom and other drugs in combination. This is particularly needed for cannabis, caffeine, and kava, as these appear to be used in combination with kratom at higher rates than other substances. Further, kratom administration was based on participants' usual products and typical doses, which varied considerably, and did not include a placebo condition. Indeed, variations in kraalkaloids across products have been observed (Leksungnoen et al. 2022) and were observed within the present study (see Study Drug section), and it is unclear if these alkaloids display a high degree of inter-subject variability between kratom users. Our substudy only examined plasma concentrations for one timepoint, and although

driving behaviors did not change, there was no control group (i.e., placebo condition) limiting the interpretation of the driving behaviors following administration. Therefore, future studies should investigate the behavioral effects of kratom across multiple doses using a placebo-controlled, within-subject design, following fixed dosing times, and utilizing repeated blood sampling methods to assess full pharmacokinetic and pharmacodynamic profiles of kratom alkaloids. Lastly, our driving simulator outcomes, while not exhaustive, are validated indicators of impairment across multiple domains. Domains not explored here should be examined in future investigations.

For now, the practical implications of this study are limited, as findings are comprised of self-report from regular consumers and of driving simulation data from a small substudy sample, all of whom self-selected into these kratom studies. Subjective ratings of impairment via self-report may be prone to bias, either consciously by overly favorable attitudes about kratom and minimizing of negative effects, or unconsciously. Our objective findings supported consumers' perceptions of driving ability confidence. Yet, this was a small substudy. We view these preliminary findings as a starting point for future work by first establishing that consumers do report routinely driving after using kratom, but without perceived or evinced intoxication. With respect to the objective findings, they are for now best viewed as proof-of-concept, not the final word and should be assessed with caution that these results may not translate to all populations.

However, it is reasonable to conclude that among these adults who use commercial kratom products regularly, we found no decrease in self-reported driving confidence following kratom self-administration, nor did we find evidence of objective impairment in driving behavior or performance following self-administration of kratom doses typical for each participant. Further research is necessary to better understand the potential effects of kratom on driving and other daily activities among those who use kratom regularly and among people who are kratom naïve. Forensic data on impaired driving related to kratom use remains scarce even as kratom use has increased significantly since 2015 and even as many regular users report driving contemporaneous to using kratom. As driving is common among people who use kratom as part of daily living and kratom users and products are heterogenous, additional research is needed to determine the boundary conditions under which kratom may produce functional impairment.

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Disclosure statement

KED has consulted for Mind Med, Della Terra, and DemeRx and been on advisory boards/steering committees for Cessation Therapeutics and Indivior. KES has been a paid scientific advisor to the International

Plant and Herbal Alliance. All authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

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