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Outpatient Management of Complicated Polysubstance Use Disorder with Kratom Dominance Using the MATRIX Program: A Case Series from Thailand

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Case Report

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Abstract

Background

Kratom (*Mitragyna speciosa*) was decriminalised in Thailand in August 2021, followed by the Kratom Plant Act 2022. Despite growing accessibility, clinical data on the outpatient management of kratom use disorder with co-occurring psychiatric comorbidities remain scarce.

Objective

To describe the clinical presentations, treatment approaches, and outcomes of three patients with kratom use disorder managed in an outpatient addiction psychiatry setting.

Methods

A retrospective case series of three male patients presenting to an outpatient psychiatric clinic between July and November 2023. All received structured biopsychosocial treatment using the MATRIX Intensive Outpatient Program, combined with brief interventions, motivational interviewing, cognitive-behavioural therapy (CBT), and relapse prevention. Pharmacotherapy was individualised according to comorbidity.

Results

All three patients (ages 19–24) with complex psychiatric comorbidities reported six-month kratom abstinence using the MATRIX Intensive Outpatient Program and individualised pharmacotherapy. Abstinence was based on self-report and clinical evaluations, as standard immunoassay panels do not detect kratom alkaloids and no mitragynine-specific testing was performed.

Conclusions

A structured outpatient biopsychosocial program, combined with targeted pharmacotherapy, may facilitate kratom abstinence in patients with complex psychiatric comorbidities. Clinicians should remain alert to emerging primary psychiatric disorders that may be masked or precipitated by kratom and polysubstance use.

Introduction

Kratom (*Mitragyna speciosa* Korth.), a plant indigenous to Southeast Asia, has been used for centuries in Thailand as a traditional stimulant and analgesic, particularly among agricultural workers. Its main alkaloids, mitragynine and 7-hydroxymitragynine, act on opioid, adrenergic, serotonergic, and

dopaminergic receptors, with predominantly stimulant effects at low doses and opioid-like sedation and analgesia at higher doses [1], [2].

Thailand decriminalised kratom on 24 August 2021 by removing it from the Schedule V Narcotic Drugs list, and the Kratom Plant Act 2022 came into force on 27 August 2022, establishing a legal framework for cultivation, sale, and consumption [3]. Under this legislation, the sale of kratom leaf and naturally prepared kratom tea is permitted; however, mixing kratom with other controlled substances (the so-called “4x100” preparation combining kratom with cough syrup), as well as sale to persons under 18 years of age, pregnant women, and breastfeeding mothers, remains prohibited.

Following decriminalisation, surveillance data have revealed concerning trends in youth kratom use. A 2022 Bangkok behavioural surveillance survey of 5,740 students found past-year kratom use prevalence of 9.3% (95% CI 8.7–9.9%), with significantly higher rates among males (12.4%) compared to females (6.1%, $p < 0.001$) [4]. Multivariable analysis demonstrated strong associations between kratom use and lower academic performance, with adjusted odds ratios of 2.41 (95% CI 1.76–3.29) for medium GPA and 4.15 (95% CI 2.94–5.87) for low GPA, as well as with cannabis use (AOR = 6.84, 95% CI 4.61–10.15) and illicit opioid use (AOR = 8.13, 95% CI 4.35–15.18) [4].

Despite legalisation, kratom use disorder presents a growing clinical challenge. Users may consume several litres of kratom tea daily and experience withdrawal symptoms including insomnia, irritability, myalgia, and autonomic instability upon cessation [5]-[7]. Kratom use is frequently complicated by polysubstance use and co-occurring psychiatric disorders including depressive episodes, anxiety disorders, and, in severe or prolonged cases, psychosis [8]. Neurological complications such as seizures have also been reported [9].

Existing literature has characterised kratom’s opioid-like dependence mechanism, withdrawal syndrome, and epidemiology in Southeast Asia [5]-[9], and several reviews and case series have addressed pharmacotherapy and psychosocial approaches to management [10]-[15]. Smith et al. identified ongoing controversies in the assessment, diagnosis, and treatment of kratom use disorder, noting the paucity of Southeast Asian clinical data and the absence of reports on structured intensive outpatient approaches [15]. Individual pharmacotherapy case reports include methadone substitution in adolescent populations [16] and treatment with a tricyclic antidepressant [17]. However, the literature does not describe the application of structured multicomponent outpatient programs such as the MATRIX Intensive Outpatient Program to kratom use disorder, and there are no published case series describing this clinical context following decriminalisation in Thailand.

Clinical evidence to guide the management of kratom use disorder in Thailand, particularly in patients with polysubstance use and co-occurring psychiatric comorbidities, remains limited. We present a case series of three patients treated in an outpatient addiction psychiatry clinic following Thailand’s 2021 decriminalisation of kratom. Co-occurring polysubstance use in all three cases prevents attribution of outcomes specifically to kratom use disorder treatment alone; this limitation is addressed explicitly in the Limitations section. Nevertheless, this series extends existing reviews: it documents real-world

presentations in a post-decriminalisation Southeast Asian context; it reports the first application of the MATRIX Intensive Outpatient Program (IOP) to kratom use disorder; it describes the individualised pharmacotherapy decisions, including benzodiazepine-facilitated withdrawal management and low-dose opioid agonist therapy, that clinicians face in the absence of randomised evidence; and it presents a three-year longitudinal trajectory (Case 3) documenting progression from kratom use disorder to schizophrenia.

Methods

Study Design and Setting

This is a retrospective case series. Three patients with kratom use disorder presenting consecutively to the outpatient psychiatric clinic of Rajavithi Hospital between July and November 2023 were included.

Treatment Protocol

Treatment Protocol
All patients received standardised biopsychosocial treatment comprising

- Brief advice and brief intervention
- Motivational interviewing (MI)
- Cognitive-behavioural therapy (CBT) for substance use
- Relapse prevention planning
- MATRIX Intensive Outpatient Program (biopsychosocial model) [11]

We assessed the stage of change using the Transtheoretical Model [12]. We selected pharmacotherapy based on presenting symptoms and comorbid diagnoses. We followed up patients at regular outpatient visits and by telephone.

Ethical Considerations

We obtained written informed consent from all patients for anonymous publication of their clinical information. Patient identifiers have been removed or altered to protect confidentiality. This case series was conducted in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committee of Rajavithi Hospital (approval no. 157/2569).

Case Reports

Case 1: Kratom Use Disorder with Mild Depressive Episode and Suicidal Ideation

The patient presented with a superimposed mild depressive episode and passive suicidal ideation following six years of high-volume kratom use; demographics, intake quantities, and polysubstance history are summarised in Table 1. Pharmacotherapy consisted of clonazepam 0.5 mg nightly and clorazepate for withdrawal management, diclofenac for withdrawal-related myalgia, with fluoxetine 20 mg daily added at the second visit following withdrawal stabilisation; mood stabilised rapidly. The patient adopted lemon tea (1 litre/day) as a behavioural harm-reduction substitute for kratom tea, a culturally acceptable strategy that appeared to support sustained abstinence. At six months, he maintained complete kratom abstinence confirmed across seven telephone contacts, and reduced cigarette use from 40 to 6–7 per day.

Table 1
Clinical characteristics and outcomes of three patients with kratom use disorder

Characteristic	Case 1	Case 2	Case 3
Age / sex	21 years / male	19 years / male	24 years / male
Education	Bachelor's degree	Non-formal upper secondary	Bachelor's degree
Occupation	Company employee	Vendor	Unemployed
Age at first substance use	15 years (kratom)	Not specified	13 years (tramadol)
Duration of kratom use	6 years	About 2 months (mixed with cough syrup)	9 years
Kratom quantity at intake	4 L/day	3 L/day (with cough syrup)	Boiled leaf: 40 leaves/5 L per week
Other substances	Ketamine, cannabis, cigarettes, alprazolam, benzhexol	Cannabis, cigarettes	Tramadol, cannabis, cigarettes
Presenting complaint	Self-referred for abstinence; mood instability, suicidal ideation	Generalised tonic-clonic seizure after kratom ingestion	Self-referred; cognitive symptoms and catatonic features after cessation
ICD-10 diagnosis	F19.3, F32.0	F19.2	F19.2, F19.74
Psychosocial treatment	MATRIX program	MATRIX program	MATRIX program
Pharmacotherapy	Clonazepam, clorazepate, diclofenac, fluoxetine	Lorazepam, methadone (7 days), sertraline	Fluoxetine and risperidone; risperidone stopped at visit 2; risperidone 3 mg restarted at schizophrenia diagnosis
Outcome at 6 months	Kratom-free; cigarettes reduced to 6–7/day	Kratom-free after a lapse (visit 2) and a two-week relapse (visit 5)	Kratom-free; schizophrenia diagnosed three years later

ICD-10: International Classification of Diseases, 10th Revision; F19.2: dependence syndrome due to multiple drug use; F19.3: withdrawal state due to multiple drug use; F19.74: other persisting cognitive impairment due to multiple drug use; F32.0: mild depressive episode.

Case 2

Kratom Use Disorder Presenting with Seizure Following Kratom-Cough Syrup Ingestion and History of ADHD

A 19-year-old male with untreated ADHD and learning disability presented following a witnessed generalised tonic-clonic seizure attributed to kratom-cough syrup (“4x100”) ingestion, which prompted voluntary treatment-seeking six days later (Table 1). Pharmacotherapy included lorazepam 1 mg for acute withdrawal management (discontinued by visit 3 as withdrawal symptoms resolved), sertraline 50 mg for mood stabilisation, and low-dose methadone 5 mg once daily initiated at visit 1 for 7 days to address opioid-like kratom dependence. Although the patient had no prior illicit opioid use history, methadone was selected because mitragynine, kratom’s primary active alkaloid, acts as a partial mu-opioid agonist and produces physical dependence amenable to opioid substitution therapy. A single sip of kratom at visit 2, followed by a two-week relapse at visit 5 (500-1,000 mL/day), was addressed within a non-punitive relapse-as-learning-event framework. At visit 6, the patient’s mother independently confirmed sustained behavioural improvement; telephone follow-up over seven contacts confirmed complete kratom abstinence at six months.

Case 3: Kratom Use Disorder with Cannabis-Induced Cognitive Impairment, Catatonic Features, and Subsequent Schizophrenia Diagnosis

The patient presented with post-cessation catatonic features, cognitive slowing (MoCA 23/30), and paranoid ideation following prolonged polysubstance use (Table 1); CT brain showed no structural abnormality. Fluoxetine 20 mg and risperidone 1 mg were commenced; risperidone was discontinued at the second visit after paranoid ideation had largely resolved, raising the possibility of substance-induced, self-remitting psychosis, and the patient was maintained on fluoxetine monotherapy across visits 2–8 with no overt psychotic features. Three years after achieving kratom abstinence, he returned with renewed catatonic features and behavioural disorganisation in the confirmed absence of substance use; thorough re-evaluation established a diagnosis of schizophrenia and risperidone 3 mg was reinstituted, indicating the need for longitudinal psychiatric follow-up even after abstinence is achieved.

Results

Summary of Clinical Characteristics and Outcomes

All three patients reported kratom abstinence at six months. Table 1 summarises the clinical characteristics and outcomes.

Table 1
Summary of clinical characteristics and outcomes of three patients with kratom use disorder.

Characteristic	Case 1	Case 2	Case 3
Age / Sex	21 years / Male	19 years / Male	24 years / Male
Education	Bachelor's degree	Non-formal upper secondary	Bachelor's degree
Occupation	Company employee	Vendor	Unemployed
Age of first use	15 years (kratom)	Not specified	13 years (tramadol)
Duration of kratom use	6 years	~ 2 months (mixed)	From age 15
Kratom quantity at intake	4 L/day	3 L/day (+ cough syrup)	Boiled leaf: 40 leaves/5 L per week
Polysubstance use	Ketamine, cannabis, cigarettes, alprazolam, benzhexol	Cannabis, cigarettes	Tramadol, cannabis, cigarettes
Presenting complaint	Self-referred, sought abstinence; mood instability, SI	Generalised tonic-clonic seizure post-kratom ingestion	Self-referred; cognitive symptoms, catatonic features post-cessation
ICD-10 diagnosis	F19.3, F32.0	F19.2	F19.2, F19.74
Psychosocial program	MATRIX program	MATRIX program	MATRIX program
Pharmacotherapy	Clonazepam, Clorazepate, Diclofenac, Fluoxetine	Lorazepam, Methadone (visit 1, for 7 days), Sertraline	Fluoxetine + Risperidone 1mg (visit 1); Risperidone discontinued at visit 2; Fluoxetine monotherapy (visits 2–8); Risperidone 3mg restarted at readmission (schizophrenia diagnosis)
Outcome at 6 months	Kratom-free; cigarette reduced to 6–7/day	Kratom-free; brief lapse (visit 2) and two-week relapse (visit 5), then sustained abstinence	Kratom-free; later diagnosed schizophrenia

ICD-10: International Classification of Diseases, 10th Revision; F19.2: dependence syndrome due to multiple drug use; F19.3: withdrawal state due to multiple drug use; F19.74: other persisting cognitive impairment due to multiple drug use; F32.0: mild depressive episode.

Table 2
Clinical course and management of Case 1

Time point	Clinical findings	Management
Visit 1	Self-referred for abstinence after six years of kratom tea use (4 L/day); mild depressive episode with passive suicidal ideation; concurrent ketamine, cannabis, alprazolam, benzhexol, and cigarette use (40/day)	Clonazepam 0.5 mg at night and clorazepate for withdrawal; diclofenac for myalgia; MATRIX program with MI, CBT, and relapse prevention
Visit 2	Withdrawal symptoms stabilised	Fluoxetine 20 mg daily added
Visit 3	Mood improving; kratom tea replaced with lemon tea (1 L/day)	Behavioural substitution reinforced
Six months	Kratom abstinence reported across seven telephone contacts; cigarettes reduced to 6–7/day	Continued telephone follow-up

MI: motivational interviewing; CBT: cognitive-behavioural therapy.

Table 3
Clinical course and management of Case 2

Time point	Clinical findings	Management
Index event	Witnessed generalised tonic-clonic seizure about 2.5 hours after drinking a kratom and cough syrup mixture ("4x100") of unknown composition	Emergency department care
Visit 1 (6 days after seizure)	Voluntary presentation, motivated to stop; background of untreated ADHD and learning disability; concurrent cannabis and cigarette use	Lorazepam 1 mg; methadone 5 mg once daily for 7 days; MATRIX program with MI, CBT, and relapse prevention
During treatment	Mood symptoms requiring stabilisation	Sertraline 50 mg for mood stabilisation
Visit 2	Single sip of kratom (lapse)	Addressed non-punitively as a learning event
Visit 3	Withdrawal symptoms resolved	Lorazepam discontinued
Visit 5	Two-week relapse (kratom with cough syrup, 500-1,000 mL/day)	Relapse reviewed as a learning event; relapse prevention plan updated
Visit 6	Abstinent for one month; mother reported less gaming, reduced tobacco use, restored sleep, and new non-using peer group	Family involvement continued
Six months	Kratom abstinence reported across seven telephone contacts	Continued telephone follow-up

ADHD: attention-deficit/hyperactivity disorder; MI: motivational interviewing; CBT: cognitive-behavioural therapy.

Table 4
Clinical course and management of Case 3

Time point	Clinical findings	Management
Visit 1	Catatonic features, cognitive slowing (MoCA 23/30), and paranoid ideation after stopping prolonged kratom and polysubstance use; CT brain without structural abnormality	Fluoxetine 20 mg and risperidone 1 mg; MATRIX program with MI, CBT, and relapse prevention
Visit 2	Paranoid ideation largely resolved	Risperidone discontinued; fluoxetine continued
Visits 2–8	No overt psychotic features; kratom abstinence	Fluoxetine monotherapy
Three years later	Renewed catatonic features and behavioural disorganisation; no substance use	Diagnosis of schizophrenia; risperidone 3 mg restarted

MoCA: Montreal Cognitive Assessment; CT: computed tomography; MI: motivational interviewing; CBT: cognitive-behavioural therapy.

Treatment Adherence and Follow-Up

All three patients demonstrated good treatment adherence, attended scheduled outpatient visits, and responded to telephone follow-up contacts. Case 1 completed seven telephone follow-up contacts, Case 2 completed seven telephone follow-up contacts, and Case 3 completed eight clinic visits before the extended follow-up period that culminated in the schizophrenia diagnosis.

Urine drug screening at initial presentation confirmed each patient's reported substance use history and did not reveal additional illicit substances beyond those acknowledged. Standard immunoassay panels do not detect kratom alkaloids; therefore, follow-up urine drug screening was performed primarily to monitor for concomitant illicit drug use rather than to confirm kratom abstinence. Follow-up urine immunoassays for morphine, amphetamine, and cannabis were negative at scheduled outpatient visits. The composition of the cough syrup consumed during Case 2's relapse was unknown; a negative morphine immunoassay would exclude a codeine-containing preparation but not dextromethorphan- or antihistamine-based products, which standard panels do not detect. Because standard panels do not detect ketamine or all benzodiazepines, these results cannot exclude use of such substances. Abstinence from kratom was monitored primarily through self-report and, in Case 2, collateral history from the patient's mother.

Discussion

Overview of Findings

This case series describes three distinct clinical trajectories of kratom use disorder managed in an outpatient addiction psychiatry clinic in Thailand. Presentations ranged from depression with suicidal

ideation, through a neurological emergency, to post-cessation cognitive impairment. Despite this heterogeneity, all three patients reported sustained kratom abstinence with a structured biopsychosocial approach supplemented by targeted pharmacotherapy.

Epidemiological Context: Youth Prevalence and Risk Correlates in Post-Decriminalisation Thailand

The present cases emerged in the context of Thailand's 2021 decriminalisation and the subsequent Kratom Plant Act 2022. As outlined in the Introduction, the 2022 Bangkok survey linked adolescent kratom use with male sex, lower academic performance, and concurrent cannabis and illicit opioid use [4].

These epidemiological findings directly inform the present series. Case 2, a 19-year-old male with a history of ADHD and learning disability whose childhood ADHD treatment was discontinued because of financial constraints, illustrates the developmental vulnerability for substance use among youth with untreated neurodevelopmental disorders and lower educational attainment. The strong association between kratom use and polysubstance use observed in the Bangkok survey is reflected in all three cases, each of whom reported concurrent use of cannabis, cigarettes, and other substances.

Product Safety and Contamination Risks

As kratom products have diversified, product quality and adulteration have become growing public health concerns [18]. Analyses of kratom teas purchased via food delivery platforms in Thailand revealed inconsistent alkaloid content and frequent contamination with other psychoactive drugs, including antihistamines, ketamine, and stimulants [10]. This contamination increases the risk of unexpected adverse events and complicates clinical attribution of symptoms and complications.

Case

's consumption of "4x100", a colloquial Thai term for a cocktail of kratom decoction mixed with codeine- or dextromethorphan-based cough syrup, cola, and ice, named after the approximate cost (100 Thai baht) of its original ingredients, illustrates this risk. The seizure that precipitated his emergency department presentation occurred two and a half hours after consuming approximately half a glass of kratom tea; however, the product's precise composition, including the presence of codeine, dextromethorphan, or other cough syrup constituents, was unknown. It is therefore possible that psychoactive contaminants or co-ingested cough syrup constituents, not kratom alkaloids alone, contributed to both the acute seizure and the subsequent mental health complications observed in this case, and this cannot be excluded as a confounding factor. Vendor-purchased kratom decoctions in Southeast Asia are frequently of variable and uncharacterised composition, and the potential for synergistic toxicity between kratom alkaloids and undisclosed additives points to the need for systematic product testing and quality control measures.

Pharmacotherapy for Kratom Use Disorder: Emerging Evidence

Clinical evidence to guide pharmacotherapy for kratom use disorder remains limited, with most data derived from case reports and small case series. This series contributes to this emerging evidence base by documenting clinical outcomes from individualised pharmacotherapy tailored to comorbid psychiatric conditions.

Case 1

was managed with benzodiazepines (clonazepam, clorazepate) for withdrawal symptoms and fluoxetine for comorbid depression. The patient's self-initiated abrupt cessation and rapid mood stabilisation following the addition of fluoxetine suggest that structured pharmacotherapy for comorbid depression may facilitate engagement with psychosocial treatment.

The role of benzodiazepines in kratom use extends beyond management of co-occurring anxiety or psychiatric disorders. Kratom withdrawal produces opioid-like features: anxiety, insomnia, restlessness, myalgia, and autonomic instability that overlap with the GABAergic dysregulation seen in sedative-hypnotic withdrawal. Case reports describe the use of benzodiazepines as a symptomatic measure for kratom withdrawal [14], [15]; however, this practice has not been evaluated in controlled studies. In Case 1, benzodiazepines were prescribed for withdrawal symptom relief alongside fluoxetine for comorbid depression, and it is not possible to attribute improvement selectively to either agent. This case nonetheless illustrates that kratom withdrawal management may require pharmacotherapy targeting both opioid-like physical symptoms and affective comorbidities.

Case 2

was managed with lorazepam for withdrawal symptoms, sertraline for mood stabilisation, and methadone 5 mg once daily, initiated at presentation and maintained for seven days before discontinuation. The rationale for short-term opioid agonist-assisted withdrawal management despite the absence of prior illicit opioid use was the established partial mu-opioid agonist activity of mitragynine, which produces a physical dependence syndrome clinically analogous to opioid use disorder [15]. The use of methadone in this case is consistent with emerging case reports describing opioid agonist substitution for kratom use disorder, particularly in adolescent populations [13], [16]. A Veterans Affairs case series reported safe buprenorphine/naloxone induction as early as eight hours after last kratom use, with maintenance doses sometimes up to 24 mg/day for prolonged symptoms [19]. Although this series did not use buprenorphine/naloxone, the observed tolerability of low-dose methadone (5 mg daily) in Case 2 is consistent with the feasibility of short-term opioid agonist-assisted withdrawal management for kratom use disorder even in the absence of prior opioid use history.

In Case 3, early discontinuation of risperidone was followed by a long symptom-free interval on fluoxetine alone. The eventual diagnosis of schizophrenia at a later readmission reflects the diagnostic

complexity inherent to prolonged polysubstance exposure and the importance of longitudinal psychiatric follow-up.

Published clinical guidance notes that evidence for pharmacotherapy of kratom use disorder is sparse and largely limited to case reports and small series [15], [20]. Whether kratom use disorder should be conceptualised and treated from an opioid use disorder (OUD) perspective remains debated; given that mitragynine acts as a partial mu-opioid agonist, opioid agonist therapies are pharmacologically plausible and supported by emerging case evidence [13], [15], [16]. However, kratom's pharmacology extends beyond opioid receptors: mitragynine also engages adrenergic alpha-2, serotonergic 5-HT2A (antagonist), and dopaminergic D1 pathways [1], [20], suggesting that opioid-receptor-targeted pharmacotherapy alone may not fully address all dimensions of kratom dependence. The largest published case series to date documented 28 patients with kratom use disorder treated with long-term buprenorphine, achieving 82% negative mitragynine testing at 12 weeks using liquid chromatography mass spectrometry [25]. The present series adds to this evidence base by documenting outcomes with individualised pharmacotherapy including low-dose methadone for opioid-like physical dependence (Case 2) and benzodiazepines for withdrawal symptom management (Cases 1 and 2) in a context where no randomised evidence exists.

Psychosocial Interventions: The MATRIX Program

The MATRIX Intensive Outpatient Program, originally developed for stimulant use disorders and supported by multisite randomised controlled trial evidence [24], provided a consistent programmatic scaffold incorporating psychoeducation, CBT, motivational enhancement, family involvement, and relapse prevention [11]. Its adaptation for kratom use disorder in the Thai context appears clinically feasible and should be investigated further.

All three patients in this series received the MATRIX program as the core psychosocial intervention, supplemented by brief interventions, motivational interviewing, and relapse-prevention planning. The program's emphasis on family involvement was particularly relevant in Case 2, where the patient's mother independently confirmed behavioural change at visit 6, noting reduced video gaming, reduced tobacco use, restored sleep, and a shift to older peer groups who did not use kratom.

There are no controlled trials of standardised psychosocial protocols for kratom use disorder in published literature. Survey research on kratom users has likewise identified a need for rigorous epidemiologic and clinical studies [21]. The present series provides preliminary evidence supporting the feasibility and acceptability of the MATRIX program for kratom use disorder.

Case 1: Depression, Suicidality, and Harm Reduction

Case 1

shows the co-occurrence of kratom dependence with a depressive episode and passive suicidal ideation, a combination demanding concurrent management of affective symptoms alongside withdrawal and

relapse prevention.

The use of lemon tea as a behavioural substitute for kratom tea may represent a culturally acceptable harm reduction strategy. The patient reported substituting kratom intake with lemon tea (1 litre/day) by visit 3, and this substitution appeared to support sustained abstinence. Behavioural substitution strategies replacing the ritual and sensory aspects of substance use with non-pharmacological alternatives are well-established harm reduction approaches in addiction treatment and may be particularly relevant in the Thai cultural context, where tea consumption is a common social practice.

Case 2

Seizure as a Motivational Catalyst and the Role of Relapse as a Learning Event

Case 2

introduces a rare but clinically important complication: a generalised tonic-clonic seizure following ingestion of a kratom-cough syrup ("4x100") mixture of unknown composition. Although seizures have been reported in kratom toxicity, in this case the neurological event itself motivated treatment-seeking. The patient presented voluntarily for addiction treatment six days after the seizure, expressing concern about his seizure and a motivated desire to stop kratom use.

The patient's brief lapse at visit 2 and subsequent two-week relapse at visit 5 (kratom mixed with cough syrup at 500-1,000 mL per day), followed by sustained recovery, illustrate the utility of relapse as a learning event within a harm reduction framework. At visit 6, the patient had been abstinent for one month following the relapse, and his mother independently confirmed behavioural change. This trajectory aligns with the Transtheoretical Model's view of behaviour change as a non-linear process involving multiple cycles of action, relapse, and re-engagement [12].

The background of untreated ADHD and learning disability in childhood is noteworthy as a developmental vulnerability for substance use. The patient was treated in primary school (Grade 5), but his ADHD treatment was discontinued because of financial constraints. This case points to broader systemic barriers in Thai healthcare access and the importance of addressing neurodevelopmental disorders as part of comprehensive addiction treatment.

Case 3: Cannabis, Kratom, and the Diagnostic Complexity of Substance-Induced Psychosis

Case 3

illustrates the diagnostic ambiguity inherent to substance-induced psychosis in the context of heavy polysubstance use. Attributing the post-cessation catatonic and paranoid features to cannabis- or kratom-related neurotoxicity initially appeared reasonable, as these features remitted during sustained abstinence. Three years later, renewed catatonic and disorganised features emerged in the confirmed

absence of substance use, leading to a definitive schizophrenia diagnosis, consistent with Danish registry data showing that approximately one-third of individuals with substance-induced psychosis convert to schizophrenia or bipolar disorder, with the highest risk following cannabis-induced psychosis [22], and with a subsequent meta-analysis reporting a pooled conversion rate of 25% overall and 34% for cannabis-induced psychosis [23]. This case highlights the need for longitudinal psychiatric follow-up beyond the achievement of abstinence.

Limitations

Limitations of this series include the small sample size, retrospective design, lack of standardised rating scales for systematic outcome measurement, reliance on self-report for abstinence (though Case 2 had collateral confirmation from his mother), and the single-centre context. All three patients presented with co-occurring polysubstance use and/or psychiatric comorbidities; this precludes any causal attribution of outcomes specifically to kratom use disorder treatment, as improvements may reflect treatment of co-occurring conditions, natural history, or non-specific therapeutic factors. Conclusions are therefore best understood as describing real-world clinical management of complex presentations rather than the efficacy of kratom-specific interventions. Although urine drug screening was performed at each outpatient visit and was negative for the opioids, amphetamines, and cannabis tested, standard immunoassay panels do not detect kratom alkaloids; kratom abstinence therefore rested on self-report and, in Case 2, collateral history, limiting objective verification of kratom-specific abstinence. The lack of systematic hepatic function monitoring, neuroimaging, or cognitive assessment at follow-up visits represents a missed opportunity to detect subclinical adverse effects. The absence of a control group precludes causal attribution of outcomes to the MATRIX program or specific pharmacotherapies.

The Thai cultural and healthcare context limits generalisability, as do the specific characteristics of the patient population (all male, all presenting voluntarily, all with at least upper secondary education) and the availability of the MATRIX program and specific pharmacotherapies. The role of cultural factors, including the traditional acceptance of kratom use in Thai society and family involvement in treatment, may limit applicability to other settings.

Clinical Implications and Future Directions

Despite these limitations, the series offers practical lessons for managing kratom use disorder in post-legalisation Thailand. First, a structured biopsychosocial program such as the MATRIX IOP appears feasible and should be evaluated prospectively, ideally alongside pharmacotherapy matched to comorbid conditions. Second, seizures or other neurological events should prompt evaluation for polysubstance toxicity or product contamination, reinforcing the need for product quality control. Third, psychiatric follow-up should continue after abstinence, because primary psychiatric disorders may emerge later, particularly after early-onset or prolonged cannabis and polysubstance exposure. Finally, low-cost harm-reduction measures, such as behavioural substitution and treating relapse as a learning event, together with youth-focused prevention, may support sustained recovery.

Future research priorities include prospective, multi-centre studies with standardised outcome measures to establish evidence-based guidelines for the management of kratom use disorder; randomised controlled trials of pharmacotherapies (e.g., buprenorphine/naloxone, methadone, naltrexone) and psychosocial interventions (e.g., MATRIX program, contingency management); systematic hepatic function monitoring, neuroimaging, and cognitive assessment to detect subclinical adverse effects; product testing and surveillance to characterise alkaloid content and contamination in commercially available kratom products; and longitudinal cohort studies to characterise the natural history of kratom use disorder and the risk of conversion from substance-induced psychosis to primary psychotic disorders.

Conclusion

Kratom use disorder presents with diverse psychiatric comorbidities that require individualised assessment and targeted pharmacological intervention alongside structured psychosocial treatment. The MATRIX Intensive Outpatient Program, combined with motivational interviewing, CBT, relapse prevention, and appropriate pharmacotherapy, was associated with self-reported kratom abstinence across three patients with markedly different clinical profiles. Clinicians should maintain a high index of suspicion for emerging primary psychiatric disorders, particularly psychosis, in patients with histories of prolonged polysubstance use. They should provide long-term psychiatric follow-up beyond the achievement of abstinence.

Structured outpatient programs should be evaluated prospectively in Thailand and other countries where kratom is used or legalised. Product safety and quality control measures, youth-focused prevention programs, and systematic surveillance of adverse effects are essential public health priorities in the post-decriminalisation era.

Declarations

Ethics Approval and Consent to Participate

This case series was conducted in accordance with the Declaration of Helsinki and approved by the Research Ethics Committee of Rajavithi Hospital, Bangkok, Thailand (Ethics Approval Number: 157/2569).

Competing Interests

The authors declare no competing interests.

Consent for Publication

We obtained written informed consent from all three patients to publish anonymised clinical information.

Use of AI-Assisted Tools

During preparation of this manuscript, the authors used Grammarly for language editing and reference checking. The authors reviewed and edited all content and take full responsibility for the accuracy and integrity of the final text.

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Author Contribution

P.S. and R.P. provided clinical management of all three patients. J.N. conceptualised the study, collected and curated the clinical data, reviewed the literature, and wrote the manuscript. All authors reviewed and approved the final manuscript for submission.

Data Availability

The data supporting this case series are not publicly available to protect patient confidentiality. De-identified information is available from the corresponding author on reasonable request, subject to ethics committee approval.

References

1. Hassan Z, Muzaimi M, Navaratnam V, et al. From Kratom to mitragynine and its derivatives: physiological and behavioural effects related to use, abuse, and addiction. Neurosci Biobehav Rev. 2013;37(2):138–51.
2. Swogger MT, Walsh Z. Kratom use and mental health: a systematic review. Drug Alcohol Depend. 2018;183:134–40.
3. iLaw Thailand. Kratom Plant Act B.E. 2565 (Kratom Plant Act 2022). Available at: https://www.ilaw.or.th/articles/4846 [Accessed October 2026].
4. Thepthien BO, Jayasvasti I, Ham E. The prevalence of kratom use and association with co-occurring substance use among adolescents: a 2022 Bangkok behavioural surveillance survey, Thailand. J Ethn Subst Abuse 2026 Apr-Jun;25(2):490–504. doi: 10.1080/15332640.2024.2367233. Epub 2024 Jun 20. PMID: 38900672.
5. Galbis-Reig D. A case report of kratom addiction and withdrawal. Wis Med J. 2016;115(1):49–52.
6. Fluyau D, Revadigar N. Biochemical benefits, diagnosis, and clinical risks evaluation of kratom. Front Psychiatry. 2017;8:62.

7. Singh D, Müller CP, Vicknasingam BK. Kratom (Mitragyna speciosa) dependence, withdrawal symptoms and craving in regular users. Drug Alcohol Depend. 2014;139:132–7.
8. Eastlack SC, Cornett EM, Kaye AD. Kratom pharmacology, clinical implications, and outlook: a comprehensive review. Pain Ther. 2020;9(1):55–69.
9. Nelsen JL, Lapoint J, Hodgman MJ, et al. Seizure and coma following kratom (Mitragyna speciosa Korth) exposure. J Med Toxicol. 2010;6(4):424–6.
10. Tokuda Y, Tubtimrattana A, Tansrisawad N, Meesilpavikkai K, Thirati P. Beyond mitragynine: composition survey and stability assessment of kratom tea ordered via food delivery platforms in Bangkok, Thailand. Chula Med J. 2024;68(2):113–23. 10.56808/2673-060X.5408.
11. MATRIX Institute. The MATRIX Intensive Outpatient Treatment Model. Los Angeles, CA: MATRIX Institute on Addictions; 2004.
12. Prochaska JO, DiClemente CC. Stages and processes of self-change of smoking: toward an integrative model of change. J Consult Clin Psychol. 1983;51(3):390–5.
13. Stanciu CN, Gnanasegaram SA, Ahmed S, et al. Kratom withdrawal: a systematic review with case series. J Psychoact Drugs. 2019;51(1):12–8.
14. Sablaban IM, Gautam M. The diagnosis of severe obsessions in the setting of kratom withdrawal and treatment with lorazepam: case report. J Addict Dis. 2021;39(1):138–9.
15. Smith KE, Epstein DH, Weiss ST. Controversies in assessment, diagnosis, and treatment of kratom use disorder. Curr Psychiatry Rep. 2024;26(9):487–96. 10.1007/s11920-024-01524-1.
16. Kamaludin NN, Noor MAM, Muhamad R, Badrin ZMY, Nawi NIM. Kratom dependence in adolescents: is methadone a lifesaver? Bangladesh J Med Sci. 2021;20(3):673–7. 10.3329/bjms.v20i3.52816.
17. Vento AE, De Persis S, De Filippis S, et al. Case report: treatment of kratom use disorder with a classical tricyclic antidepressant. Front Psychiatry. 2021;12:640218. 10.3389/fpsyt.2021.640218.
18. Aly S, Grundmann O. A review of kratom product evolution and its associated health outcomes. Subst Abuse Rehabil. 2026;17:606821. 10.2147/SAR.S606821.
19. Lei J, Butz A, Valentino N. Management of kratom dependence with buprenorphine/naloxone in a veteran population. Subst Abus. 2021;42(4):497–502. 10.1080/08897077.2021.1878086.
20. Swogger MT, Smith KE, Garcia-Romeu A, et al. Understanding kratom use: a guide for healthcare providers. Front Pharmacol. 2022;13:801855.
21. Garcia-Romeu A, Cox DJ, Smith KE, Dunn KE, Griffiths RR. Kratom (Mitragyna speciosa): user demographics, use patterns, and implications for the opioid epidemic. Drug Alcohol Depend. 2020;208:107849. 10.1016/j.drugalcdep.2020.107849.
22. Starzer MSK, Nordentoft M, Hjorthøj C. Rates and predictors of conversion to schizophrenia or bipolar disorder following substance-induced psychosis. Am J Psychiatry. 2018;175(4):343–50.
23. Murrie B, Lappin J, Large M, Sara G. Transition of substance-induced, brief, and atypical psychoses to schizophrenia: a systematic review and meta-analysis. Schizophr Bull. 2020;46(3):505–16. 10.1093/schbul/sbz102.

24. Rawson RA, Marinelli-Casey P, Anglin MD, et al. A multi-site comparison of psychosocial approaches for the treatment of methamphetamine dependence. Addiction. 2004;99(6):708–17. 10.1111/j.1360-0443.2004.00707.x.
25. Broyan MV, Brose SW, Meyer JM, Kale N, Slack MS, Stanciu CN. Long-term buprenorphine treatment for kratom use disorder: a case series. J Addict Dis. 2022;40(4):516–22. 10.1080/10550887.2022.2060704.