

Research Article

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## Effects of red and pale green variety of *Catha edulis* on liver and kidney of human consumers in Meru county, Kenya

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### Abstract

*Catha edulis* (miraa) is a large green shrub that grows at high altitudes. It is a well-known tree in Kenya. The leaves of the *C.edulis* plant contain alkaloids structurally related to amphetamine and they are currently chewed daily by a high proportion of the adult population in Kenya for the resulting pleasant mild stimulant action. The habit of *C.edulis* chewing is widespread in Kenya especially in *C.edulis* producing areas and this poses a public health problem. This study was conducted to compare the effects of red and pale green variety of *Catha edulis* on human consumers in Meru County. Blood was collected from 198 *Catha edulis* chewers and 193 non-chewers. Liver biochemical parameters were affected by the red variety *Catha edulis* chewing which was shown by increased activity of alanine aminotransferase (ALA), total bilirubin (TB) and alkaline phosphatase (ALP) as compared to the pale green variety. Renal biochemical parameters were not affected. In conclusion, red variety *Catha edulis* is more potent than the pale green variety hence responsible for hepatic toxicity but not renal toxicity.

**Abbreviations:** AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase; ALP, Alkaline Phosphatase; TB, Total Bilirubin.

### Keywords

*Catha edulis* (miraa),  
Kidney,  
Liver

### Introduction

The regular consumption of *Catha edulis* is associated with a variety of health problems affecting the consumers (World Health Organization, 2012). The WHO (2003, 2006) reported that *Catha edulis* consumption has become a common problem that affects

the health aspects of life (S.kassim, S.Islam, 2010). Different varieties of *Catha edulis* have different degrees of pharmacological action. In Yemen farmers recognize four varieties based on the colour of shoots and growing twigs as 'Abyadh' predominantly pale green in colour,

'Azraq' purplish, 'Aswad' crimson and 'Ahmar' an intermediate between 'Azraq' and 'Aswad' reddish. In Ethiopia two prominent cultivars have been described as dimma (red) and ahde (pale green) (Al-Motarrebetal., 2002; Krikorian, 1984). In Yemen forty kinds of khat were recognized by Ramadan *et al.*, (1981). Like opium, the alkaloid content of khat varies with the soil, climatic conditions, and cultivation. *Catha edulis* quality is rated by connoisseurs in a manner similar to tea and coffee. The criteria utilized depend upon the part of the plant that will be used – leaves, buds, or twigs. This is coupled with the degree of maturity, the size of the leaf and the area of plant origin. Larger and older leaves will be tough and not easily chewed and they contain a lower amount of cathinone as compared to younger leaves from the same plant. In addition, the red leaf type known as "dimma" is known to have more cathinone than the pale green leaf type known as "dallota". Khat varies in strength from region to region. Kenyan khat is considered to be the strongest and, thus, the most popular (Neil, 2007).

In Meru Kenya, farmers recognize different varieties of *Catha edulis* based on their pigmentation. Kiraagikiiru (pale green), kigwe (gikieru), Muchuri, kithaara and kilantune (red).

The names such as kangeta and giza commonly encountered in markets denotes grades of miraa and do not refer to a particular tree type. The grading is based on the length of the twigs harvested. Kangeta refers to twigs of miraa of length 20-30 cm. anything shorter than this is referred to as giza (kisa). Mbaine is a kimeru word for any miraa tree dating back to over three centuries and does not refer to any particular traditional variety of miraa. The younger trees of miraa are locally known as Mithairo (Carrier, 2007).

Kangeta and giza type of miraa are sold locally and dry within two days. Leboi type which has very high moisture content is exported because it can last for 4-5 days before drying. Leboi type is considered inferior to kangeta and giza type (NACOSTI 1996).

The widespread use and popularity is due to its CNS-stimulating phenylpropylamines, especially to cathinone ( -aminopropiophenone, 'natural amphetamine') and to a much lesser extent to norpseudoephedrine ('cathine') and norephedrine (Kalix, 1988). Currently, *Catha edulis* is illegal in the USA, Canada, and many European countries (Roelandt *et al.*, 2011).

There is no study that has been done comparing the effect of different varieties of *Catha edulis* on kidney

and liver of human consumers in this region. This study compared the effect of red and pale green variety of *Catha edulis* on kidney and liver function in human.

## Materials and Methods

### Samples Collection

The study was approved by the Kenyatta National Hospital/University of Nairobi – Ethical Review committee (KNH/UoN-ERC) through the ministry of health. The study was carried out in Meru County, which is found in Eastern region of Kenya, approximately 225 km Northeast of the capital, Nairobi. It covers a geographical area of 6,936 sq.kms with a population of 1,365,301 according to 2009 population census of Kenya (KNBS, 2015). Purposive sampling method was used to select four out of nine constituencies in the Meru County. Convenient-consecutive sampling technique was used to randomly recruit all accessible and consenting *C. edulis* chewers and non-chewers. Also "snowball sampling technique" (getting *Catha edulis* chewers to refer those they know, these individuals in turn refer those they know and so on) which greatly hastened participants' recruitment.

The selection of participants was based on the following inclusion and exclusion criteria: Participants were *Catha edulis* chewers and non-chewers at the age above 18 years and below 61 years. Persons with diabetes, cardiovascular diseases, renal problems, hepatitis, hypertension, glomerulonephritis, HIV positive and pregnant women were excluded from the study.

A total of 391 participants were enrolled into the study (198 *Catha edulis* chewers and 193 non-chewers). A structured self-administered questionnaire was used for data collection. The questionnaire covered a range of socio-demographic characteristics and data on *C. edulis* chewing (amount of *Catha edulis* per day, number of bundles per week and number of years of chewing), alcohol drinking, hypertension, diabetes and any family history of liver problem and kidney problem. *Catha edulis* non-chewers with no family history of liver problem and kidney problem were also enrolled for the study. Written consent was taken from all the participants after explanation of the aim of the study.

### Sample collection

Blood samples were collected from the arm by venipuncture using an evacuated tube collection system. Five milliliters of blood was collected into a plain vacutainer without anticoagulant and allowed to clot.

The clot samples were centrifuged immediately for 10 minutes at 3000 rpm. After centrifugation, the serum was separated and transferred to clean vials with the help of pipette. The vials containing serum were transported to Biochemistry laboratory, Nyeri provincial hospital to analyze biochemical parameters.

### Biochemical Analysis

Biochemical parameters were analyzed in 10 µl aliquots of serum by auto-analyzer (Human Star 200, Human Diagnostic Worldwide, GmbH, Germany). Biochemical parameters included total bilirubin (TB), direct bilirubin (DB), alkaline phosphatase (ALP), albumin (ALB), alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea (Ur) and creatinine (Cr).

I-smart 30 electrolyte analyzer was used to analyze the electrolytes.

Serum remaining after testing, used needles and syringes and vacutainers were destroyed through incineration.

### Data analysis

The acquired data by the researcher was analyzed using descriptive and inferential statistics. Statistical Package for Social Sciences (SPSS) version 21 was employed in the entry and analysis of data. Results were expressed as mean ± SD values and as number and percentage values for categorical data. Comparison between red variety chewers, pale green variety chewers and non-chewers was done using the one way ANOVA test, followed by the post-hoc Tukey test. The significance level was set at =0.05.

### Results

#### Demographic characteristics of the study participants

Among age group 18-30 years 46% chewed the red type and 55.6% chewed the pale green type of *Catha edulis*. Majorities (56%) of chewers chewed the red variety of *Catha edulis* and are in age group 31-40; followed by chewers in age group 18-30 (55.6%) who chewed the pale green variety of *Catha edulis* (Table 1).

**Table 1: Demographic characteristics of the study participants**

| Variable         | chewers |    |                     |      |                            |      |
|------------------|---------|----|---------------------|------|----------------------------|------|
|                  | Total   |    | Red variety chewers |      | Pale green variety chewers |      |
|                  | n       | %  | n                   | %    | n                          | %    |
| <b>Gender</b>    |         |    |                     |      |                            |      |
| Male             | 192     | 97 | 103                 | 53.6 | 89                         | 46.4 |
| Female           | 6       | 3  | 5                   | 41.7 | 1                          | 8.3  |
| <b>Age group</b> |         |    |                     |      |                            |      |
| 18-30            | 92      | 47 | 42                  | 46   | 54                         | 55.6 |
| 31-40            | 62      | 31 | 35                  | 56   | 27                         | 44   |
| >40              | 44      | 22 | 31                  | 29.0 | 13                         | 30   |

#### Distribution of the study participants by age and variety of *C. edulis* chewed

Figure 1 shows distribution of the study participants by age and variety of *Catha edulis* chewed.

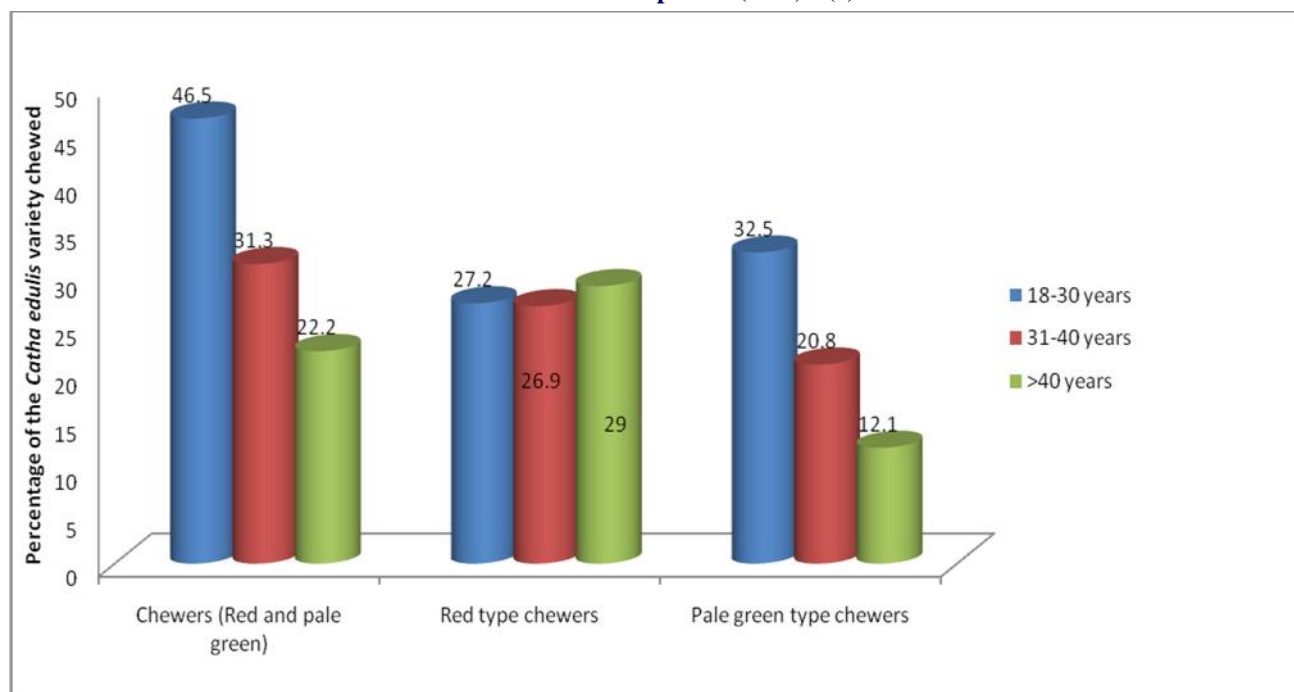


Figure 1: Distribution of the study participants by age and variety of *C. edulis* chewed

**Distribution of the study participants by *C.edulis* chewing habit**

With reference to the red type of *C.edulis* majority (69.6%) of the participants chewed two bundles per day and for the pale green type majority (58.1%) chewed one bundle per day. The red type, majority (60.1%) chewed *C.edulis* for more than three days in a week and for the pale green type majority (58.3%)

chewed for less than three days in a week. The red type, majority (78.9%) of the participants have chewed *C.edulis* for less than one year and for the pale green type majorities (59.2%) have chewed for five to ten years. *C.edulis* chewing habit is more frequent among red variety *C.edulis* chewers group than pale green variety chewers group (54.5% vs 45.5%). The participants' *C.edulis* chewing habits are shown in Table 2.

Table 2: Distribution of the study participants by *C.edulis* chewing habit

| Characteristics<br>Variety of <i>C.edulis</i>    | Red |      | Sample size<br>pale green |      | Total |       |
|--|-----|------|---------------------------|------|-------|-------|
|  | No  | %    | No                        | %    | No    | %     |
| <b>Bundles of <i>C.edulis</i> chewed per day</b> |     |      |                           |      |       |       |
| 1  | 39  | 41.9 | 54                        | 58.1 | 93    | 46.97 |
| 2  | 48  | 69.6 | 21                        | 30.4 | 69    | 34.85 |
| 3  | 19  | 57.6 | 14                        | 42.4 | 33    | 16.67 |
| >5   | 2   | 66.7 | 1                         | 33.3 | 3     | 1.51  |
| <b>Frequency of <i>C.edulis</i> chewing</b>      |     |      |                           |      |       |       |
| >3 days per week                                 | 83  | 60.1 | 55                        | 39.9 | 138   | 69.70 |
| <3 days per week                                 | 25  | 41.7 | 35                        | 58.3 | 60    | 30.30 |
| <b>Years of <i>C.edulis</i> chewing</b>          |     |      |                           |      |       |       |
| < 1 year   | 15  | 78.9 | 4                         | 21.1 | 19    | 9.60  |
| 1-2 years  | 24  | 77.4 | 7                         | 22.6 | 31    | 15.70 |
| 3-5 years  | 19  | 57.6 | 14                        | 42.4 | 33    | 16.70 |
| 5-10 years                                       | 20  | 40.8 | 29                        | 59.2 | 49    | 24.70 |
| >10 years  | 30  | 45.5 | 36                        | 54.5 | 66    | 33.30 |

N=sample size, %= percentage

**Distribution of the study participants by alcohol drinking habit**

39.1% of the participants who chewed the red type of *C.edulis* reported consuming alcohol and 66.7% not consuming and for the participants who chewed the pale green type, 60.9% reported consuming and 33.3% not consuming. With reference to the red type of *C.edulis* majority (45.0%) of the participants consumed five to ten bottles per day and for the pale green type majority (59.3%) consumed less than five

bottles per day. Traditional brew was the most consumed (58.8%) for the participants who chewed the red type of *C.edulis* and bottled alcohol was the most consumed (56.4%) for the participants who chewed the pale green type of *C.edulis*. Majority (59.5%) of the participants who chewed the red type of *C.edulis* have consumed alcohol for less than five years while majority (78.3%) of the participants chewed the pale green type have consumed alcohol for more than ten years (Table 3).

**Table 3: Distribution of the study participants by alcohol drinking habit**

| Characteristics<br>Variety of <i>C.edulis</i>     | Red |      | Sample size<br>pale green |      | Total |       |
|---|-----|------|---------------------------|------|-------|-------|
|   | No  | %    | No                        | %    | No    | %     |
| <b>Drink alcohol</b>                              |     |      |                           |      |       |       |
| Yes   | 34  | 39.1 | 53                        | 60.9 | 87    | 43.9  |
| No  | 74  | 66.7 | 37                        | 33.3 | 111   | 56.1  |
| <b>Alcohol type</b>                               |     |      |                           |      |       |       |
| Bottled   | 27  | 52.9 | 24                        | 56.4 | 51    | 58.6  |
| Traditional                                       | 10  | 58.8 | 7                         | 41.2 | 17    | 19.5  |
| Both bottled and traditional                      | 9   | 42.8 | 10                        | 47.6 | 19    | 24.1  |
| Don't drink alcohol but chew                      | 74  | 66.1 | 37                        | 33.9 | 111   | 56.1  |
| <b>Quantity of alcohol drunk per day</b>          |     |      |                           |      |       |       |
| < 5 bottles                                       | 24  | 40.7 | 35                        | 59.3 | 59    | 67.8  |
| 5-10 bottles                                      | 9   | 45.0 | 11                        | 55.0 | 20    | 23.0  |
| >10 bottles                                       | 2   | 25.0 | 6                         | 75.0 | 8     | 9.2   |
| <b>Duration of alcohol consumption (in years)</b> |     |      |                           |      |       |       |
| <5 years  | 22  | 59.5 | 15                        | 40.5 | 37    | 42.5  |
| 5-10 years  | 10  | 37.0 | 17                        | 63.0 | 27    | 31.03 |
| >10 years   | 5   | 21.7 | 18                        | 78.3 | 23    | 26.4  |

N=sample size, %= percentage

**4.9 Mean ± standard deviation and test of significance of mean values between red variety chewers, pale green variety chewers and non-chewers.**

A one-way between groups analysis of variance was conducted to compare the effects of red and pale green variety of *Catha edulis* on human consumers. Participants were divided into three groups (red variety chewers, pale green variety chewers and non-chewers). Serum activity of alanine aminotransferase (ALA), alkaline phosphatase (ALP) and total bilirubin (TB) was statistically significantly (ANOVA p<0.05) different between groups. Post hoc Turkey test

indicated the mean of red variety chewers of ALA, ALP and TB was significantly increased than that of pale green variety chewers but they are within the normal range. Serum activity of urea (Ur), and creatinine (Cr) was statistically significantly (ANOVA p<0.05) different between groups. Post hoc Turkey test indicated the mean of red variety chewers was significantly decreased than that of non-chewers but they are within the normal range. Serum activity of total protein seemed statistically significantly different between groups (ANOVA p<0.05), however post hoc Turkey test indicated a non-significant different (p>0.05) (Table 4).

**Table 4: Mean ± standard deviation and test of significance of mean values between red variety chewers, white variety chewers and non-chewers.**

| Variable                 | Chewers (n=198) |        |       |            | Non-chewers(n=193) |             |       |      | P          | Tukey |
|--------------------------|-----------------|--------|-------|------------|--------------------|-------------|-------|------|------------|-------|
|                          | Range (min-max) | Red    |       | Pale green |                    | Non-chewers |       |      |            |       |
|                          |                 | M      | SD    | M          | SD                 | M           | SD    |      |            |       |
| TB (µmo/l)               | 2-21            | 11.01  | 6.01  | 8.86       | 4.96               | 11.97       | 8.90  | .005 | .043, .001 |       |
| DB (µmo/l)               | 0-3.42          | 2.74   | 2.87  | 2.60       | 2.69               | 2.89        | 1.91  | .601 |            |       |
| TP (g/l)                 | 66-88           | 73.45  | 15.07 | 73.36      | 23.11              | 68.73       | 17.28 | .041 |            |       |
| ALB (g/l)                | 35-52           | 52.47  | 9.96  | 49.35      | 13.34              | 49.78       | 11.43 | .093 |            |       |
| ALP (U/l)                | 80-306          | 200.88 | 78.63 | 176.92     | 110.34             | 169.50      | 169.5 | .005 | .001,.036  |       |
| ALA (U/l)                | 0-42            | 29.87  | 59.22 | 18.38      | 13.36              | 23.37       | 13.87 | .050 | .042       |       |
| ASA (U/l)                | 0-37            | 28.58  | 19.89 | 23.88      | 15.54              | 27.99       | 13.56 | .077 |            |       |
| Ur (mmol/l)              | 1.7-8.3         | 4.04   | 1.25  | 4.34       | 1.43               | 4.73        | 2.03  | .003 | .002       |       |
| Cr (µmo/l)               | 53-97           | 84.69  | 25.19 | 81.14      | 32.93              | 94.69       | 25.17 | .000 | .007,.000  |       |
| Na <sup>+</sup> (mmo/l)  | 135-155         | 139.33 | 16.37 | 140.11     | 7.33               | 141.15      | 5.00  | .301 |            |       |
| K <sup>+</sup> (mmol/l)  | 3.5-5.5         | 4.25   | .485  | 4.27       | .479               | 4.60        | .608  | .801 |            |       |
| Cl <sup>-</sup> (mmol/l) | 97-111          | 103.28 | 4.86  | 102.82     | 10.65              | 103.34      | 3.11  | .790 |            |       |

Av/sBv/sC: One way ANOVA test followed by post-hoc Tukey's test. n: sample size, M: mean, SD: standard deviation, TB: total bilirubin, DB: direct bilirubin, ALB: albumin, ALP: alkaline phosphatase, ASA: aspartate aminotransferase, Ur: urea, Cr: creatinine, Na<sup>+</sup>: sodium, K<sup>+</sup>:potassium, Cl<sup>-</sup>: chloride

## Discussion

Total bilirubin, alanine aminotransferase and alkaline phosphatase parameters mean were statistically significantly increased ( $p < 0.05$ ) in red variety chewers than pale green variety chewers. Important chemical reactions in the body are triggered by several enzymes produced in the liver. These enzymes are normally found within the cells of the liver. If the liver is damaged or injured, the enzymes spill into the blood causing elevated liver enzyme levels. Increased activity of alanine aminotransferase (ALT) in the serum suggests leakage of the enzyme into circulation from ruptured cell membranes of hepatocytes upon exposing to injury thus elevating serum ALT level in blood ((Edith *et al.*, 2010; Kim *et al.*, 2008; Rini *et al.*, 1981). This indicates hepatotoxicity due to red variety *Catha edulis* (hepatotoxicant) because this enzyme is more specific for detecting liver abnormalities since it is primarily found in the cytosol of the hepatocytes and its concentration in the liver far exceeds that in any other organ. The findings were consistent with those reported by Alamet *et al.*, (2014) where ALT and AST was significantly increased in khat users as compared to non-users also Al-Habori *et al.*, (2002) who declared that long term feeding of Khat leaves to New Zealand white rabbits elevated liver enzyme activities and lead to toxic hepatocellular jaundice.

Increased serum activity of alkaline phosphatase and total bilirubin in red variety *Catha edulis* chewers indicates a cholestatic pattern of liver function test disturbance. Increased serum activity of ALP in red variety chewers than that of pale green variety chewers, suggests leakage of the enzyme into circulation from damaged liver cells. Since total bilirubin and alanine aminotransferase were also increased, it means the increased ALP was of hepatic origin rather than bone origin.

Increased total bilirubin suggests a direct toxic effect of the red variety *Catha edulis* on liver cells leading to decreased uptake and conjugation of bilirubin and reduced secretion into bile ducts (decreased hepatic clearance) causing a build-up of bilirubin in the blood (Chiasera, 2010; F.H.Al-Hashe, I.Bin-Jaliah, 2011).

Chewers using red variety of *Catha edulis* are more vulnerable to *Catha edulis* induced liver damage as compared to pale green variety *Catha edulis* chewers. There was a statistically significantly ( $p < 0.05$ ) decrease in creatinine level in the serum of red variety chewers than non-chewers. A good balance of electrolytes, normal serum urea and decreased serum creatinine in the serum of red variety *Catha edulis* chewers is an indicator of well-functioning kidneys.

Chewers using red variety *Catha edulis*, majority (60.1%) have chewed for more than three days in a week and pale green variety chewers majority (58.3%) have chewed for less than three days per week. This shows that increased in amount of *Catha edulis* chewed may cause change in serum level of ALT, total bilirubin and ALP in *Catha edulis* chewers. This is in line with a study by Gemechi Tesso *et al.*, (2015) who demonstrated that there is a positive relationship between the increases in dose of crude extract of *Catha edulis* and the change in serum level of ASA, ALA, ALP, total bilirubin and direct bilirubin in rats treated with crude extract of khat.

Alcohol as a risk factor for liver problem was evaluated in this study. Despite the fact that 43.9 % of the chewers consumed alcohol none who had liver problem because even if ALP, ALA and total bilirubin were increased in the red variety *Catha edulis* chewers as compared to pale green variety chewers, they were all within the normal reference range.

## Conclusion

Liver biochemical parameters were affected in the red variety *Catha edulis* chewing group as compared to pale green variety *Catha edulis* chewing group, which was clearly shown by increasing serum activity of alkaline phosphatase, alanine aminotransferase, and total bilirubin. This indicates red variety *Catha edulis* is more potent than pale green variety.

Kidney biochemical parameters were not affected in the red variety *Catha edulis* chewing group which was clear by normal serum activity of urea, electrolytes and decreased creatinine activity.

## Recommendations

1. The concentration of cathinone and cathinein different varieties of *Catha edulis* in Meru County should be evaluated.
2. Health professionals should educate users about potential harms arising from *Catha edulis* use, and promoting responsible use (moderate use) of *Catha edulis* or avoid use in order to minimize negative health effects.
3. To shed light on red variety *Catha edulis* as a cause of liver problem, retrospective and prospective epidemiological studies of chronic miraa users should be initiated.

## Competing interests

The authors declare that they have no competing interests of any kind.

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