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Phytochemistry of antiulcer Plant based medicines used by Luhya people of western Kenya

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Abstract
Peptic ulcer disease is acid peptic injury of the digestive tract, resulting in mucosal break reaching the sub mucosa, it occurs in the stomach or duodenal. The aim of this study was to review the associated phytochemistry of antiulcer plant medicines used by Luhya people of Western Kenya. PubMed, Google scholar, Web of Science, and the Research Gate library. The antiulcer reported plants were 8, 4 were discussed further while 4 were not because of lack of literature on their antiulcer clinical studies. The phytochemicals identified were flavonoids, phenolic acid, tannins and oleuropein. Antiulcer activity of the plants and plant parts were associated with different phytochemical composition. The reviewers of this study recommend that these plants from Western Kenya should be investigated for their efficacy and phytochemical constituents.

Keywords: Peptic ulcer, anti-ulcer, phytochemical, gastric mucosa

Abbreviations

PUD:	Peptic ulcer disease
NSAID:	Nonsteroidal anti-inflammatory drugs
H2-RAs:	Type-2 histamine receptor antagonists
PPIs:	Proton pump inhibitors
H. pylori:	*Helicobactor pylory*
TNF-α:	Tumor necrosis factor alpha
NF-Kb:	Nuclear factor-kB
COX-2:	Cycloxygenase-2
TNF-α:	Tumor necrosis factor-α
HCl:	Hydrochloric acid

Introduction
Peptic ulcer disease (PUD) is acid peptic injury of the digestive tract, resulting in mucosal break reaching the sub mucosa [1]. Peptic ulcers occur mainly in the stomach [gastric ulcer (GU)] or proximal duodenum [duodenal ulcer (DU)] but they can also be found in the oesophagus or Meckel's diverticulum [2]. Peptic ulcer individuals are at risk of developing complications such as gastroduodenal haemorrhage, perforation, bleeding and obstruction, and mortality among patients with these complications is high.

The believed causes of peptic ulcer disease were hypersecretory acidic environment together with dietary factors or stress, alcohol and smoking [3] which changed when *Helicobacter pylori* and use of non-steroidal anti-inflammatory drugs (NSAIDs) were discovered in the second half of 20th century [4]. Estimated prevalence of peptic ulcer disease worldwide annually ranges from 19.4 to 57.0 cases per 100,000. Reported mortality rates between studies differ and are approximately 3% to 10% [5, 6]. The decrease in the estimates of prevalence and incidence of peptic ulcer disease has been reported worldwide, especially in developed countries due to a sharp decreasing trend in the incidence, rates of hospital admissions, and mortality associated with the disease in the past 20–30 years [1].

Symptoms of peptic ulcer disease are not predictable because they are non-specific. Patients with duodenal ulcers may feel hungry or have nocturnal abdominal pain. However, patients with gastric ulcers have postprandial abdominal pain, weight loss, vomiting, reduced appetite and nausea. Patients with untreated PUD are reported to have relapsing symptoms because of spontaneous healing and relapse while the causal factor *H pylori* infection or NSAID use persists. Elderly patients with peptic ulcer disease frequently show mild symptoms or asymptomatic [7, 8].

The current peptic ulcer treatment drugs are antacids such us sodium bicarbonate, aluminum hydroxide magnesium hydroxide salts [9], proton pump inhibitors (PPIs) [10], histamine-2 (H2) receptor antagonists subclass of antihistamines that include cimetidine, ranitidine, famotidine, and nizatidine [11] and antibiotics such as clarithromycin plus amoxicillin or metronidazole in cases of *Helicobacter pylori* infection [12-15]. Due to the reported side effects of these current drugs [16], a number of studies have been done on complementary and alternative therapies such as herbal therapies which are increasingly used [17, 18].

Traditional medicine plays an important role in treatment of chronic and mild disorders [19]. Plant based medicines have gained additional impact due to their natural origin and high therapeutic implications [20], they serve as herbal remedies being source of drugs also as food supplements with vitamins and minerals. Plant biogeography determines the abundance and availability of medicinal plants which in turn determine their use by local communities [21]. The review documented phytochemistry of antiulcer medicinal plants traditionally used by Luhya people of western Kenya. The Luhya people of western Kenya are mostly Bungoma, Busia, Kakamega and Vihiga counties. The main limitation of this systematic review was lack of enough data on the reviewed plants.

Fig 1: Map showing Luhya community counties of Western Kenya

2. Methods

The literature was searched systematically and the studies that reported prevalence, incidence, mortality rates of peptic ulcer disease were identified, antiulcer plant based medicines commonly used by the Luhya people in western Kenya were also identified. The studies on phytochemistry of these plants were identified. PubMed, Google scholar, Web of Science, Scopus, Science Direct and the Research Gate and Scientific Electronic Library Online from June 2020 to September 2020 library were searched for studies of human and animal subjects that were reported in English. Searches were performed independently in all the databases. Key words used for the searches were ulcer, peptic ulcer, traditional medicine, antiulcer plants, Western Kenya, Luhya communities, phytochemistry, prevalence, causes, ulcer drugs and peptic ulcer management.

All publishing years were considered (open study), and reports with information on antiulcer or medicinal plants used by Luhya people of Western Kenya were carefully screened. References contained within the results were assessed for their inclusion in the study, and continued searches were carried out on the databases using more general search words including ulcer, peptic ulcer, plant, plant species, plant part, plant extract, mode of extraction, phytochemisty and Kenya. The last search was done in September 2020. For this study, only full-text original research articles published in peer-reviewed journals, books, theses, dissertations, patents, and reports on antiulcer and phytochemistry of plants used by Luhya people of Western Kenya written in English and dated until August 2020 were included. In addition, studies reporting on individual type of peptic ulcer disease (gastric and duodenal) ulcers were included for the study was not on a specific type of peptic ulcer disease. Traditional, local and common names of the antiulcer plants were also captured. Review studies reported for these plants were excluded. Studies on the plants but not on peptic ulcer were also excluded for they did not provide any report on antiulcer. Data on phytochemistry of antiulcer plant based medicines used by Luhya people in Western Kenya were extracted from studies that fulfilled the inclusion and exclusion criteria (Fig 2).

2.1 Data Analysis

All data were entered into Microsoft Excel (MS). Descriptive statistical methods including frequencies and percentages were used to analyze data reported on antiulcer medicinal plants used by Luhya people of Western Kenya and associated indigenous knowledge. Results were presented as tables and charts.

2.2. Search strategy

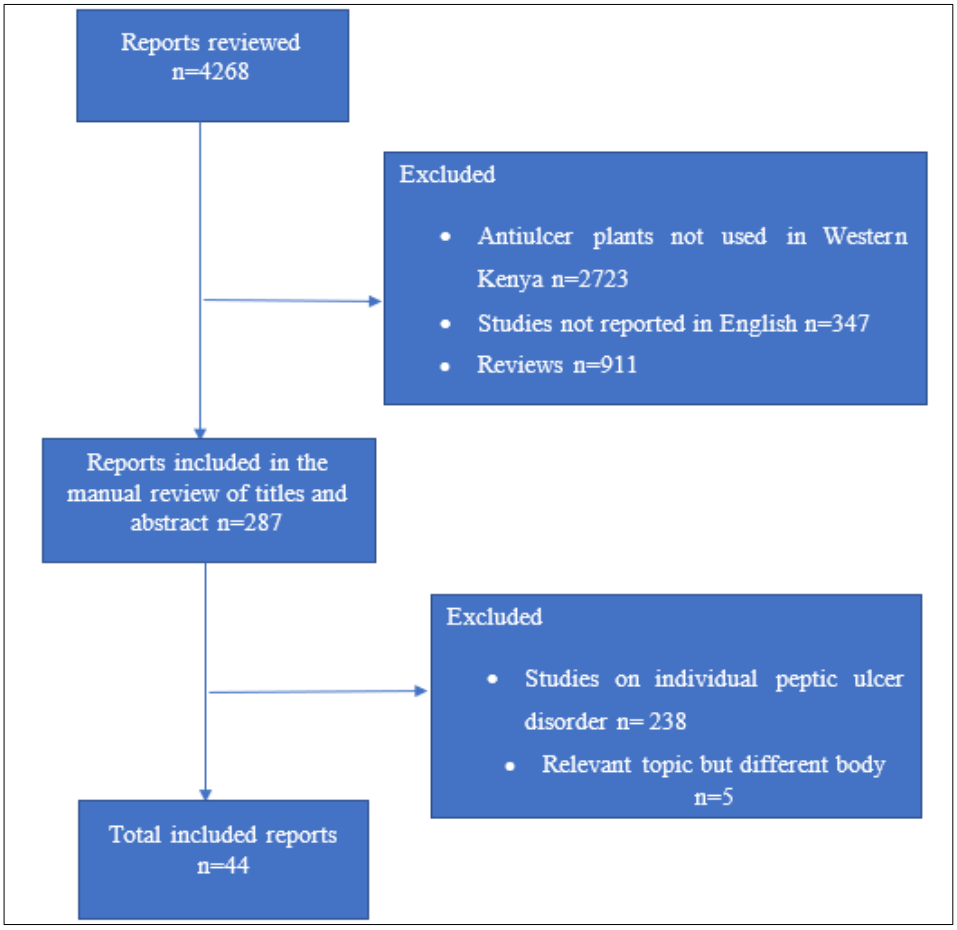


Fig 2: Flow chart of systematic literature searches conducted to identify studies that reported antiulcer treatment plants and related phytochemistry used by Luhya people of Western Kenya.

3. Results and Discussion

3.1. Antiulcer medicinal plants used by Luhya people of Western Kenya

Traditional medicines each with different associated philosophies and cultural origins are used throughout the world and herbs have been the source for most of the drugs [22, 23]. Medicinal plants contain many phytochemical compounds which are the major source of therapeutic agents for many diseases [23]. Discovery and advancement in medicinal plants have improved the health care of mankind. Some of these plant medicine remain localized while some are increasingly used in different areas of the world [24].

Studies and reports identified 8 antiulcer plant species used by Luhya people of Western Kenya belonging to different botanical families (Table 1). Oleaeceae, Gramineae, Anacardiaceae, Apiaceae, Aloeaceae, Salicaceae, and Polygonaceae the plant families of the retrieved plants. The reported species were *Olea capensis* also known as *Olea europea* [25], *Cymbopogon citratus*, *Heteromorpha trifoliate* [26], *Mangifera indica L.* [27], *Bequartiodendron oblanceolata*, *Aloe elgonica*, *Dovyalis macrocalyx* (Oliv.) Warb and *Rumex usambarensis* Jacq.

3.1.1. *Olea capensis/ Olea europea*

Olea capensis is an African tree species that belong to the olive family, Oleaceae. *Olea capensis* is a bushy shrub or a small to medium sized tree up to 10 m in height, but it may be much larger, reaching 40 m found in evergreen forest, bush and littoral scrub [28]. It's fruits take about 6 months to ripen [29] with an orthodox seed storage behavior. It is a dominant forest tree mostly known for shade. It's leaves are used tradionally for the treatment of ulcers [25].

3.1.2. *Cymbopogon citratus*

The *Cymbopogon citratus* (Lemongrass) belongs to the family Gramineae, commonly known as sweet grass family. It was named lemongrass because of typical strong lemon-like odour of the plant which has high citral content in the essential oils of this plant [30]. It was reported to be used by Luhya people of Western Kenya as antiulcer [27]

3.1.3. *Moringa indica* L.

Mango (*Mangifera indica* L.) is a national fruit. It belongs to family Anacardiaceae and highly called the "King of Fruits" [31]. Mango is a climacteric fruit and has to be harvested at physiologically mature green stage to reduce the postharvest loss [32]. The roots, leaves, fruit and bark of *Mangifera indica* (mango) have a long treatment history for wide range of conditions [33] including ulcer [27]

3.1.4. *Heteromorpha trifoliata* (H.L. Wendl.) Eckl. & Zeyh.

Heteromorpha trifoliate (L) is a member of the Apiaceae family and a deciduous shrub. Bark reddish-brown or purple-brown, smooth, peeling in papery sheets. Leaves 3-foliated or pinnate with up to 9 leaflets arranged in a variable manner, very aromatic when crushed, apex tapering to rounded, often notched; margine entire or slightly crenate [34]. Flowers small greenish or yellowish, in dense, rounded, compound umbels, appearing with the new leaves. Fruits flattened, 5-7mm long, heart-shaped, longitudinally ridge splitting in 2, pale brown when dry. It's roots have been tradionally used by Luhya people of Western Kenya as [26].

Table 1: Antiulcer medicinal plants used by Luhya people of Western Kenya

Family name	Scientific name	Local name	Common name	Plant form	Part used	Reference
Oleaeceae	*Olea capensis*	Mutukhuyu	Elgon olive	Tree	Leaves	[25, 28]
Gramineae	*Cyombopogon citrus*	Majani kho bulimo	Sweet grass	Grass	Leaves	[27, 30]
Anacardiaceae	*Mangifera indica* L.	Liembe	Mango	Tree	Bark, seeds, leaves and flowers	[27, 31, 33]
Apiaceae	*Heteromorpha trifoliate*	Mitiviazi	Carrot	Tree	Roots	[26, 34]
Not established	*Bequartiodendron oblanceolata*	Musamia	Not established	Tree	Whole plant	[25]
Aloeaceae	*Aloe elgonica*	Rodichepkukwa	Not documented	Shrub	Leaves, roots	[26]
Salicaceae	*Dovyalis macrocalyx* (Oliv.) Warb	Shinamuterwa	Not documented	Tree	Leaves, roots	[27]
Polygonaceae	*Rumex usambarensis* Jacq.	Likaachi	Dammer	Shrub	Leaves, roots	[27]

3.2. Growth habit and plant parts used for the retrieved antiulcer plants.

Antiulcer plants traditionally used by Luhya people of Western Kenya are trees (62.5%), shrubs (25%) and grass (12.5). Seemingly, trees are highly used, followed by shrubs and grass respectively (Fig 3). The commonly used parts are leaves (42.86%), roots (28.57%), whole plant (7.14), stem bark (7.14), seeds (7.14), and flowers (7.14) respectively (Fig 4). This result is similar to other studies which says that leaves accumulate more phenols and this may be related to plant leaves antiulcer activity [35, 36]

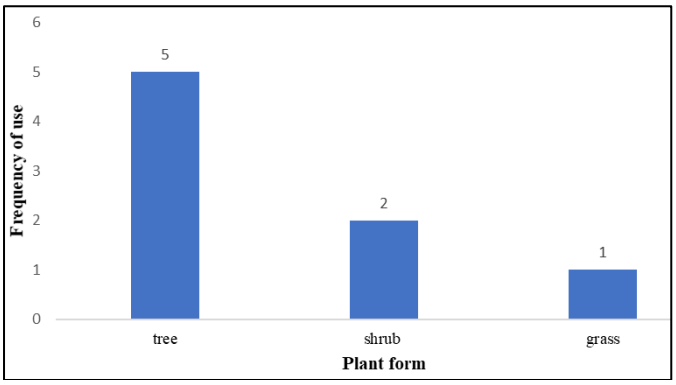


Fig 3: Frequency antiulcer plant form used by Luhya people of Western Kenya

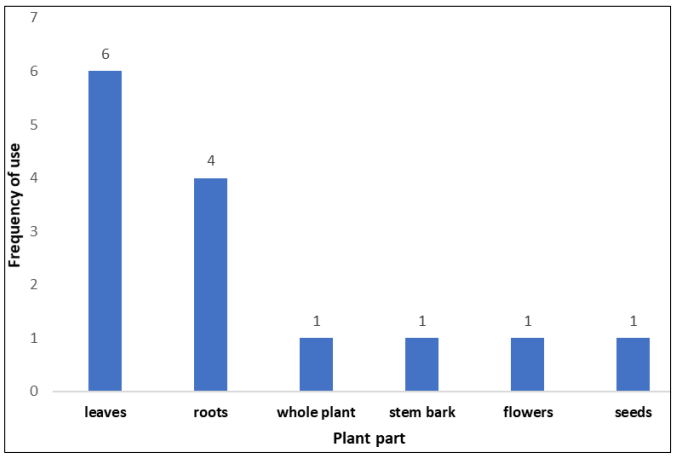


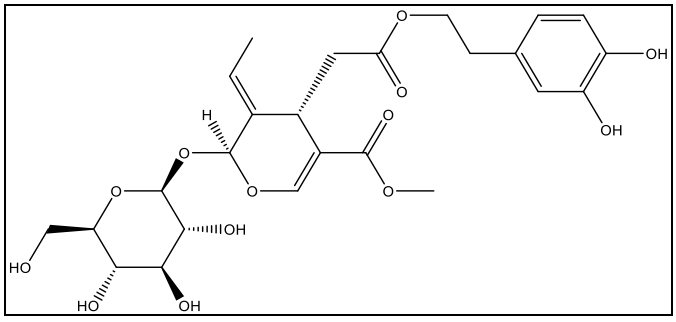
Fig 4: Frequency of antiulcer plant parts used by Luhya people of Western Kenya

3.3. Phytochemical composition of antiulcer medicinal plants used by Luhya people of Western Kenya

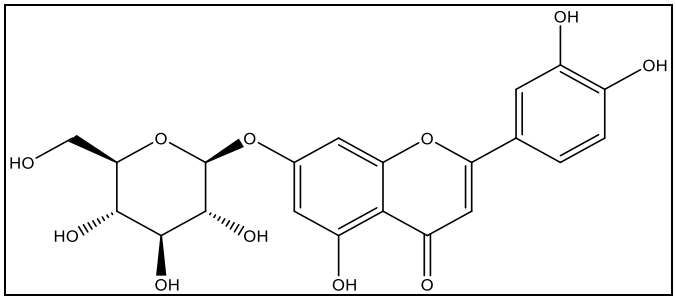
Phytochemicals are naturally occurring chemical compounds found in plants. The recent studies reveal that plants have roles in the protection of human health through food or drug intake [37, 38]. A number of phytochemicals have been studied and classified by protective function which may defer due to different extraction methods and solvents employed. Some of these plants have been subjected to clinical studies and reported to possess antiulcer activity in different regions and countries (Table 2).

3.3.1 lea europaea / capensis

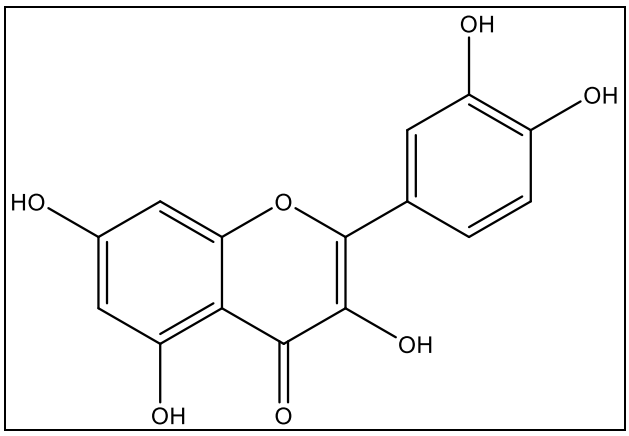
Antiulcer activity of the *Olea europaea* (Oleaceae) was investigated in rats by inducing gastric mucosal injuries by a high concentration of ethanol and antiulcer activity of Olive (Olea europaea) leaf methanolic extract investigated in rats by inducing gastric mucosal injuries by HCl and ethanol studied in Saudi Arabia and Serbia. In both tests, Olive leaf was effective in the prevention of an increase in gastric lipid peroxidation and in the prevention of a decrease in antioxidant enzyme activity and it attenuated the inflammatory response by decreasing nuclear factor-kB (NF-kB), cycloxygenase-2 (COX-2) and tumor necrosis factor-α (TNF-α) expressions which indicated that Olive leaf has gastroprotective activity against ethanol and HCl-induced gastric lesions in rats, possibly related to its antioxidant properties. These activities could be related to the phenolic compounds that were identified and quantified in the extract. The major constituent of the olive leaf extract was oleuropein (19.8%), a well-known antioxidant. The other identified components were caffeic acid, luteolin-7-O-glucoside, apigenine-7-O-glucoside, and quercetin. These constituents of the olive leaf possess antioxidant properties, which were experimentally confirmed in several studies [39-41].



a. Oleuropein



b. Luteolin 7-O-glucoside

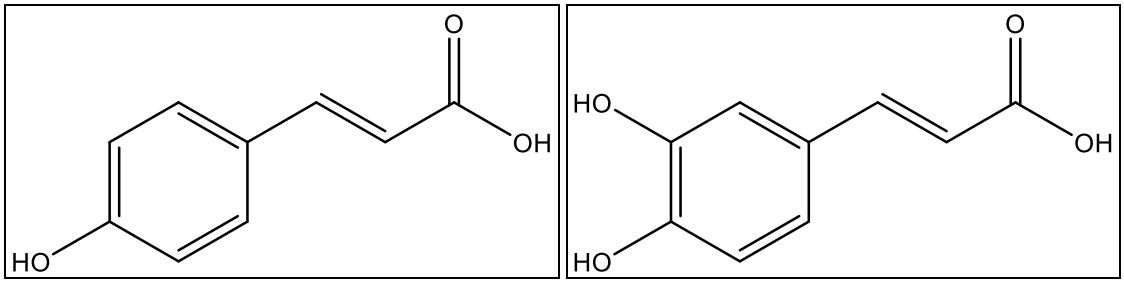


c. Quercetin

Fig 5: (a), (b), (c), structures of compounds identified in ethanolic leaf extract of *Olea europaea*

3.3.2. *Cyombopogon citrus*

Antiulcer activity of the *Cyombopogon citrus* was investigated in rats by inducing gastric mucosal injury by acute concentration of ethanol studied in Portugal. *Cyombopogon citrus* leaves significantly reduced gastric injury. The results of this assay confirmed the gastroprotective activity of *C. citratus* extract on experimental gastric lesions in rats induced by ethanol. Gastroprotective activity of *Cyombopogon citrus* leaves could be related to phytochemical compounds including tannins, phenolic acids (caffeic and p-coumaric acid derivatives) and flavonoids [42].



a. Coumaric acid b. Caffeic acid

Fig 6: (a), (b), structures of compounds identified in *Cyombopogon citrus* leaf extract

3.3.3. *Moringa indica* L

Antiulcer activity of ethanolic extract of *Mangifera indica* seed Kernel was investigated in rats by inducing gastric mucosal injury by acid ethanol in India. *Mangifera indica* seed kernel significantly reduced the ulcer index, pH, protein levels and total acidity. Gastroprotective activity of *Moringa indica* L is associated with the presence of tannins and flavonoids [43].

3.3.4. *Heteromorpha trifoliate*

In Zimbabwe antiulcer activity of *Heteromorpha trifoliata* root acceleration was investigated in rats by inducing gastric injury by acetic acid. *H. trifoliata* did not show any significant effect on gastric acid secretion stimulated by histamine, gastrin and carbachol. Thus, *H. trifoliata* accelerated the healing of acetic acid-induced peptic ulcer in rats. The associated phytochemical was not documented [44].

Table 2: Phytochemical composition of antiulcer medicinal plants used by Luhya people of Western Kenya

Plant	Country studied	Part studied	Mode of extraction	Phyto-constituent	Reference
Olea europaea / *capensis*	Saudi Arabia and Serbia	Leaves	Maceration	oleuropein	[40, 41]
Cyombopogon citrus	Portugal	Leaves	Maceration	Tannins, phenolic acids (caffeic and p-coumaric acid derivatives) and flavonoids	[42]
Moringa indica L	India	Seed kernel	Maceration	Tannins and flavonoids	[43]
Heteromorpha trifoliate	Zimbabwe	Roots	Dry powder	Not documented	[44]
Bequartiodendron oblanceolata	Not documented	Not documented	Not documented	Not documented	Not documented
Aloe elgonica	Not documented	Not documented	Not documented	Not documented	Not documented
Dovyalis macrocalyx (Oliv.) Warb	Not documented	Not documented	Not documented	Not documented	Not documented
Rumex usambarensis Jacq.	Not documented	Not documented	Not documented	Not documented	Not documented

4. Conclusion

As discussed in section 3.1, table 1, various plants species and plant parts possess antiulcer properties. We reviewed the phytochemistry that underlies this effect. Our data shows that the discussed plants and plant parts possess different kinds of phytochemicals as summarized in table 2. They include flavonoids, tannins, phenolic acids and oleuropein. These compounds were shown to be most associated with antiulcer effects as discussed in section 3.3.

5. Recommendation

The discussed antiulcer plants used by Luhya people of Western Kenya may also possess flavonoids, tannins, phenolic acids and oleuropein thus, further studies are required to isolate the active compounds in the unstudied plants. The other plants without clinical reports should also be investigated for their efficacy and phytochemical constituents.

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