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Review Article

Hematological Changes Provoked by Natural Alkaloids

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Abstract

Background and aims: Plant alkaloids are naturally occurring nitrogen-containing chemicals with a wide range of therapeutic applications. They have been reported to cure a considerable number of illnesses, including cancer, diabetes, malaria, and heart dysfunction. This study sought to evaluate the impact of several plant alkaloids on hematological parameters in animals.

Methods: The results of different plant extracts containing alkaloids in laboratory animals on hematological indices such as red blood cell (RBC) count, hemoglobin (Hb) concentration, hematocrit (Hct), white blood cell count, platelet count, and others using normal laboratory methods were gathered from scientific papers and databases using keywords such as plant alkaloids, alkaloid toxicity, hematological parameters, hematological changes, blood, and animals.

Results: Plant alkaloids identified through the search had different impacts on hematological indices. Some alkaloids raised RBC count, Hb concentration, and Hct, while others lowered these values. Platelet count was generally observed to increase, but there were exceptions. Certain alkaloids found in some plants have no substantial influence on hematological parameters.

Conclusion: Plant alkaloids can cause various changes in hematological parameters in animals. These alterations might be useful or deleterious depending on the alkaloid and its concentration. Understanding these effects is essential for the safe and effective use of plant-based therapies.

Keywords: Alkaloids, Plants, Hematological changes, Blood, Toxicity, Animals

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Introduction

Researchers were attracted in the past to work on alkaloids in plants owing to their many traditional uses. Today, these compounds are of significant value in the pharmaceutical and medicine industries (1). Several scholars have tried to define alkaloids since their discovery. Adam Friedrich Wilhelm Serturner, a splendid pharmacist, became the first to separate and isolate morphine from poppy seeds in 1805 completely. Numerous researchers have examined its chemistry and reported on its pharmacological characteristics. In 1819, Wilhelm Meifsner coined the term alkaloid. He found that alkaloids are natural alkaline and coined the term "alkaloid", which means "alkali-like substance" (2). Serturner's endeavor separated various additional alkaloids, including codeine, strychnine, emetine, veratrine, caffeine, brucine, and quinine, between 1817 and 1821. In the mid-1980s, scientists made a giant leap forward by synthesizing alkaloids. Ball made an effort to create synthetic quinine in a research laboratory. In the 1990s, Waller and co-worker Nowacki discovered many alkaloid characteristics following a series of discoveries (3). Therefore, they defined alkaloids as substances that occur naturally with a mildly alkaline composition with nitrogen atoms in their structure. Similar characteristics can be found in several alkaloids-derived semi-synthetic substances (4). In particular, the structures of alkaloids include carbon, nitrogen, and hydrogen. Also, they are made up of sulfur, bromine, oxygen, chlorine, and phosphorus.

Alkaloids are secondary metabolites of plants that are cosmopolitan in nature and present in fungi, bacteria, animals, and most notably in plants (leaf, stem, root, seed, and fruits). They can be found in almost every cell organelle, including vesicles, mitochondria, vacuoles, and chloroplasts (5). Alkaloids are found in various plant groups, with an estimated 40% having at least one species producing this metabolite. Additionally, approximately 20 000 chemicals have been investigated because of their possible biological activity; only half of them are listed in the dictionary of alkaloids; some of them, however, are well recognized for their effects on therapeutic, poisonous, stimulant, and narcotic activities (6).

Chemical Properties and Structure of Alkaloids

Alkaloids, like inorganic alkalis, are low-molecular-weight molecules with a bitter taste as nonvolatile solids that can react with acids to generate salts. In acid-base processes, these nitrogen atoms can serve as bases.

Alkaloids classified as amines typically contain the suffix -ine in their names, much like amines. These chemicals are often colorless, although numerous colored alkaloids have also been identified, such as the yellow berberine, the copper-red sanguinarine salt, and the red betanidin (7). These are crystalline solids with distinct melting points, ring structures, and bitter tastes. They are occasionally found in plants as glycosides. However, they can also exist in free form as salt or nitrogen oxides (8). The vast bulk of alkaloids also contain oxygen and carbon, hydrogen, and nitrogen atoms. A few, like nicotine from tobacco and coniine from hemlock, are oxygen-free. Strychnine hydrochloride, for example, is more easily dissolved in water than in organic solvents. However, free bases are readily soluble in organic solvents as salts. Many alkaloids are optically active (only a few are dextrorotatory) because of tertiary nitrogen in their compositions. The primary characteristic of alkaloids is a heterocyclic ring with a nitrogen atom (others are noncyclic long-chain nitrogen compounds) (8).

Nearly all alkaloids have at least one nitrogen atom, and some have more than five. They can be found as primary, secondary, or tertiary amines and monomers, dimers, trimers, or tetramers. The amino acids tryptophan, lysine, tyrosine, phenylalanine, and anthranilic acid create alkaloids. Several alkaloids are produced from ornithine through metabolic processes: The Krebs cycle, the Shikimate pathway, and glycolysis (9). The structures are shown in Figure 1.

Distribution of alkaloids

Many living organisms form alkaloids, but higher plants produce most (10%–25%). As a result, chemicals found in plants were referred to as "alkaloid" substances. Plants typically contain a few percent, or a small number, of alkaloids that are unevenly spread throughout the plant's tissues. The maximum concentration can be found in the leaves of some plants, such as black henbane, the fruits or seeds of other plants, like strychnine trees or *Rauvolfia serpentina* roots, or the bark of yet other plants (cinchona) (10). Additionally, different alkaloids may be present in various tissues of the same plants. Plants contain a variety of groupings of structurally the same alkaloids, ranging from a few numbers to over 30. The alkaloids are members of a similar class, but one of them predominates, and their structures are slightly different. Alkaloids are abundant in certain plant families. For instance, 30 different alkaloids exist in plants, like the ergot fungus (Claviceps) and the *Papaver somniferum*. The function of alkaloids in plants is still mostly unknown. The amount of alkaloids in some plants increases just before seed production. Then, it decreases once the seed reaches maturity, implying that alkaloids perform a role in this process.

In addition to being found in plants, alkaloids can also be found in animals such as *Castor canadensis*, frogs (poison dart frogs), *bufotenin* in the skin of certain toads, and fungi like *psilocybin* mostly in fungus genus *Psilocybe* as well as a variety of insects, such as ants (11). For example, indole alkaloids are abundant in sponges and fungi associated with soft corals. It has also been discovered that fungi that make indole alkaloids are hosted by other marine vertebrates, including sea stars and cucumbers. Some amines, like serotonin and adrenaline, crucial for higher animals to function, are also known as alkaloids because of their structure and biosynthesis similarities.

Pharmaceutical and medicinal application of plant alkaloids

Alkaloids revealed a wide range of medicinal properties. They are mainly well known for their therapeutic uses as anesthetics, cardio-protective and anti-inflammatory drugs. Many famous alkaloids are employed in clinical contexts, including nicotine, ephedrine, strychnine, quinine, and morphine. They also have antiviral, antimicrobial activities, anticancer, muscle relaxant, anti-platelet and anticoagulant (12), anti-hypertensive, wound healing, antirheumatic, emetic, anthelmintic, purgative (13) activities (Table 1).

Methods for hematological testing of plant alkaloids

The effects of plant alkaloids on hematological parameters in animals were tested using either manual or automated methods. Following the intervention period with the plant extract containing alkaloids, the animals were fasted overnight and anesthetized with chloroform or halothane. Blood was obtained from the animals through cardiac puncture. The blood collected was placed in tubes containing Ethylenediaminetetraacetic acid (EDTA) (14).

Manual method

The blood collected in the EDTA tube was used to estimate hematological indices. The red blood cell (RBC) number was determined using Dacie and Lewis' method. The blood was diluted to 1:200 with Hayem's fluid, which maintained the RBC intact and thereafter counted. The number was counted using a Neubauer counting chamber employing a light microscope. Brown's method determined the total number of white blood cells using a diluting fluid (Turk's fluid) in a ratio of 1:20. The packed cell volume (PCV) was calculated using the macrohematocrit procedure. The blood's hemoglobin (Hb) content was estimated using Sahli's hemoglobinometer (14). To determine platelet count, a small quantity of diluted whole blood was mixed with a red cell lysing reagent like ammonium oxalate, placed in a hemocytometer, and platelets were counted employing phase-contrast light microscopy. Thereafter, the dilution factor was applied to the count (15,16). Mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and mean corpuscular volume (MCV) were calculated from values of RBC, PCV, and Hb as follows:

MCH (pg) = Hb (g /dL) × 10 / RBC count (15)

MCHC (g /dL) = Hb (g /dL) × 100 / PCV (%) (15)

MCV (fL) = PCV (%) × 10 / RBC count (15)

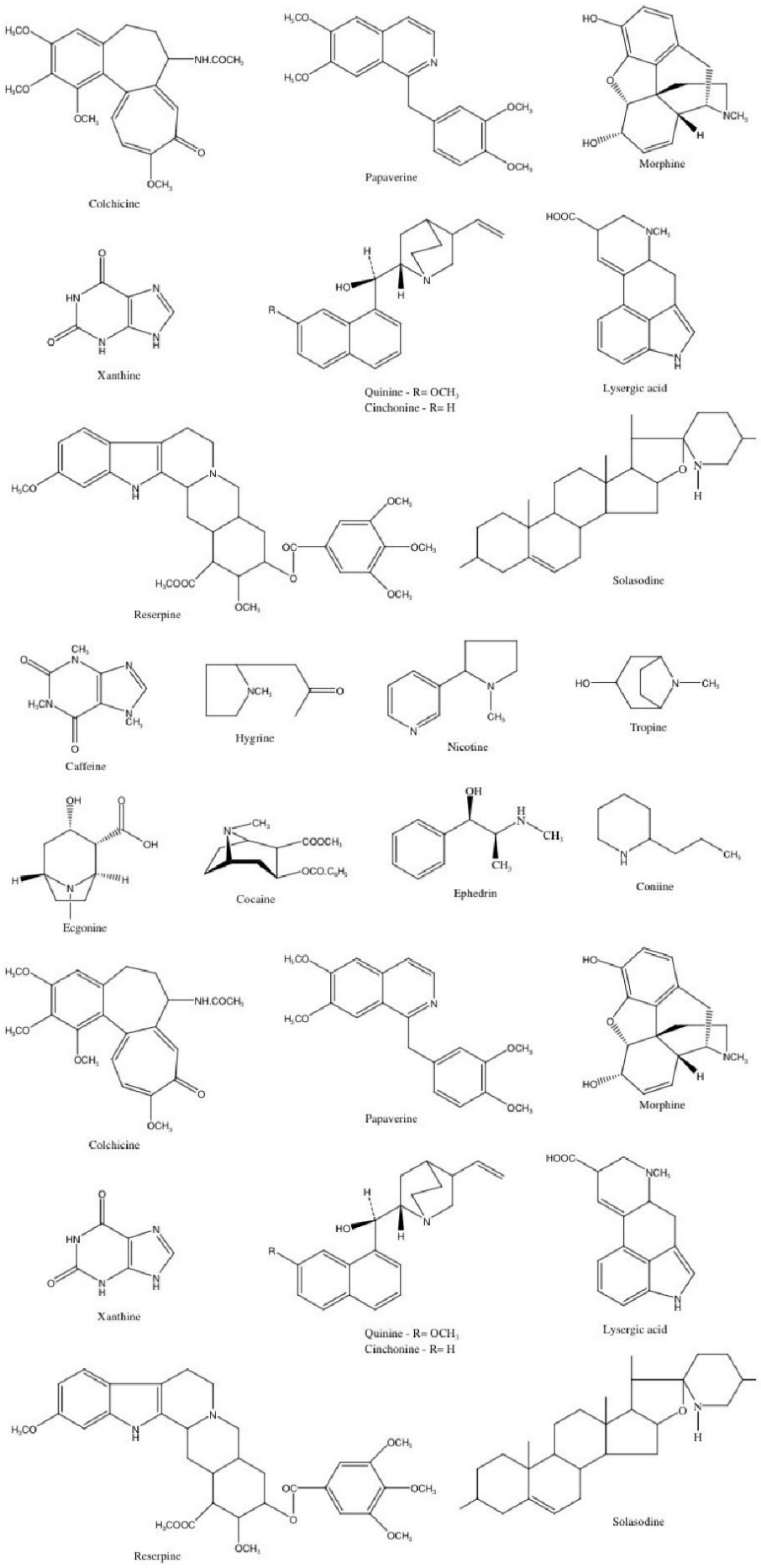

Figure 1. Chemical structure of some plant alkaloids. Adapted from: http://www.studocu.com/ (2022)

Table 1. Summary of the pharmaceutical and medicinal uses of plant alkaloids

Alkaloid	Pharmaceutical uses
Morphine and strychnine	Analgesic and narcotics
Caffeine and strychnine	Angina treatment and CNS stimulants
Vincristine, vinblastine and taxol	Anti-cancers
Atropine	Causes mydriasis and bradycardia
Eserine and pilocarpine	Myotics
Ephedrine	Anti-asthmatics
Codeine	Antitussives, analgesic
Emetine	Emetics, Intestinal amoebiasis
Reserpine	Anti-hypertensives
Atropine and papaverine	Relaxation of smooth muscle, anti-Parkinson
Tubocurarine	Relaxation of skeletal muscle
Pelletierine and arecoline	Anthelmintics
Quinine and emetine	Relaxation of smooth muscle
Cocaine	Local anesthetic

Automated method

A Mindray hematology analyzer was used to analyze blood collected in EDTA-containing tubes (BC2800 vet). Total RBC, Hb concentration, hematocrit (Hct), total leucocyte count (WBC), platelet counts, mean platelet volume, MCH, MCHC, and MCV were all determined (17).

Alkaloids and hematological changes

Blood is an essential body fluid comprising blood plasma and blood cells. Approximately 45% of blood includes blood cells, and 55% is plasma. Erythrocytes, leukocytes, and thrombocytes are these blood cells. Erythrocytes are nucleated blood cells that comprise around 45% of all blood and contain Hb, essential for carrying carbon dioxide away from the body's cells and distributing oxygen to its various cells (17). Leukocytes are another crucial element of the immune system that are important for getting rid of pathogens, abnormal cellular debris, and other foreign substances from the body. The blood coagulation process depends on thrombocytes, also called platelets. These blood cells are essential hematological components necessary for healthy bodily function.

These hematological parameters can deviate from their normal ranges for various reasons, which can have adverse effects (18). Animals' hematological parameters have been found to change in response to some phytochemical constituents, such as flavonoids, saponins, and alkaloids (19). Alkaloids in medicinal plants are known to cause diverse changes in hematological indices in laboratory animals. Some are known to either increase or decrease hematological parameters, while others cause no change (Table 2).

Plant alkaloid nicotine in *Nicotiana tabacum* is reported to decrease hematological indices like RBC count, Hb concentration, and Hct but cause an increase in white blood cell (WBC) count and platelet count (14). The significant decrease in PCV, RBC, Hb, MCV, and MCH when compared with the control group shows that nicotine has adverse hematologic effects. An explanation for this is that nicotine produces peroxidants when metabolized in the body, and these peroxidants cause oxidative damage to the erythrocyte membrane, leading to hemolysis of the cell. The recurring hemolysis that occurs with continuous use of nicotine and subsequent peroxidation explains the cause of the decrease in Hb concentration, PVC, and other RBC parameters (Tables 3, 4, and 5) (14).

Moreover, when 40 mg/kg of the methanol leaf extract of *Crotalaria lachnosema Stapf.* (MLECL) was administered daily orally in rats for six weeks, there was a significant drop in hematological indices, such as RBC, Hb, and Hct counts. This finding suggests that MLECL, which contains the low-dose alkylating chemical pyrrolizidine alkaloid (nucleotoxic), may have a depressive impact on the red cell lines in the bone marrow, limiting hematopoietic function (20).

Gongronema latifolium was revealed to contain alkaloids through phytochemical analysis (21). The oral administration of ethanol root extract from the plant was reported to cause some hematological changes. The extract was observed to cause little or no change in RBC count, PVC, MCV, and MCH. However, low doses of the extract statistically elevated the Hb concentration. In contrast, high doses elevated WBC count significantly owing to a rise in monocyte and eosinophil counts. MCHC was dose-dependently decreased (21).

Interestingly, various parts of *Datum stramonium* have been demonstrated to be toxic and employed for medicinal purposes. It consists of many alkaloids, the most prominent of which are scopolamine and hyoscyamine. The extract of the plant was demonstrated to cause alteration in hematological indices. It significantly increased Hb concentration, PVC, RBC, WBC, and MCV, while there was a decline in the values of MCH and MCHC in treated West African Dwarf (WAD) bucks. The results show that the alkaloids in the extract had no adverse effects on the animals. The higher WBC count indicated that the WAD bucks have a functioning immune system that proffers excellent health (22).

Sole administration and pre-treatment of rats with ethanolic leaf extract of *Moringa oleifera* before administering nicotine were reported to cause a significant increase in the RBC, PCV, Hb, MCV, and MCH, as depicted in Tables 3 and 4. The group given concurrent nicotine and Moringa extract had a significantly lower ($P<0.05$) RBC count when compared with both the untreated and nicotine control groups. RBC, PVC, Hb concentration, and other red cell parameters significantly increased ($P<0.05$) in the nicotine-treated group after post-treatment with the Moringa extract compared to the nicotine control group. The leukocyte levels did not change substantially in any of the treated groups. The platelet level increased statistically ($P<0.05$) in all test groups except

Table 2. Some medicinal plants containing alkaloids and their hematological effect

Plant	RBC	WBC	PVC	Hb concentration	Platelet	MCHC	MCV	MCH
Gongronema latifolium	No change	Increased in both doses	Increased in low dose	Increased in high dose	-	Increased in high dose	No change	No change
Eugenia jambolana	No change	No change	No change	No change	No change	-	-	-
Haloxylon salicornicum	Increased	-	Increased	Increased	-	Increased	Decreased	Increased
Moringa oleifera	Increased	-	Increased	Increased	Increased	No change	Increased	Increased
Maerua crassifolia	No change	No change	No change	No change	No change	No change	No change	No change
Datum stramonium	Increased	Increased	Increased	Increased	-	Decreased	Increased	Decreased
Carpobrotus edulis	No change	No change	No change	No change	No change	No change	No change	No change
Nicotiana tabacum	Decreased	Increased	Decreased	Decreased	Increased	No change	-	No change
Crotalaria lachnosema	Decreased	-	Decreased	Decreased	-	-	-	-
Ipomea batata	Increased	Increased	Increased	Increased	Decreased	Increased	Increased	Increased in low dose but decreased in high dose
Luffa cylindrica	No change	No change at low dose, Increased at high dose	No change	No change	No change at acute level Increased at sub-chronic level	-	No change	-

Table 3. Results of the effect of ethanolic extract of *Moringa oleifera* leaves on nicotine-induced changes in red blood cell count, packed cell volume, and hemoglobin concentration

Group	RBC ($\times 10^6$)/mm^3		PCV (%)		HB concentration (g /dL)	
	Week 2	Week 4	Week 2	Week 4	Week 2	Week 4
A (untreated control)	5.28 ± 0.102	4.94 ± 0.192	40.40 ± 1.600	35.40 ± 0.812	13.12 ± 0.488	12.08 ± 0.644
B (nicotine control)	4.17 ± 0.159[a]	4.35 ± 0.168	30.80 ± 2.222[a]	34.80 ± 2.154	10.32 ± 0.628[a]	11.88 ± 0.745
C (moringa pre-treatment)	5.38 ± 0.172[b]	4.73 ± 0.263	41.60 ± 1.860[b]	39.80 ± 2.417	13.60 ± 0.856[b]	13.36 ± 0.699
D (concurrent moringa and nicotine)	3.58 ± 0.250[ab]	3.65 ± 0.171[ab]	34.33 ± 2.729	35.33 ± 1.453	10.60 ± 0.693[a]	11.47 ± 0.751
E (moringa posttreatment)	4.04 ± 0.183[a]	5.32 ± 0.158[b]	29.40 ± 2.657[a]	43.80 ± 2.200[ab]	11.68 ± 0.554	14.13 ± 0.418[b]
F (moringa only)	5.37 ± 0.190[b]	5.47 ± 0.244[b]	41.00 ± 2.073[b]	47.20 ± 1.772[ab]	13.28 ± 0.731[b]	15.32 ± 0.609[ab]

Abbreviations: RBC, Red blood cell; PCV, packed cell volume; HB, hemoglobin.
Values are expressed as the mean ± standard error of the mean. [a] Significantly different from the untreated control group at $P < 0.05$; [b] Significantly different from the nicotine control group at $P < 0.05$.
Source: Bamidele et al (14).

Table 4. Results of the effect of ethanolic extract of *Moringa oleifera* leaves on nicotine-induced changes in mean cell volume, mean cell hemoglobin, and mean cell hemoglobin concentration

Group	MCV (cu.μ)		MCH (pg)		MCHC (%)	
	Week 2	Week 4	Week 2	Week 4	Week 2	Week 4
A (untreated control)	76.42 ± 2.193	71.88 ± 2.185	24.81 ± 0.577	24.42 ± 0.842	32.56 ± 1.106	34.12 ± 1.668
B (nicotine control)	73.70 ± 3.728	79.73 ± 2.187[a]	24.81 ± 1.544	27.22 ± 0.719	33.75 ± 1.540	34.15 ± 0.536
C (moringa pre-treatment)	77.21 ± 1.217	84.30 ± 2.925[a]	25.18 ± 0.881	28.48 ± 1.781[a]	32.61 ± 1.014	33.72 ± 1.314
D (concurrent moringa and nicotine)	95.79 ± 1.587[ab]	96.99 ± 4.728[ab]	29.93 ± 2.909[ab]	31.42 ± 1.715[ab]	31.36 ± 3.483	32.65 ± 2.965
E (moringa post-treatment)	72.88 ± 6.307	82.24 ± 2.372[a]	28.98 ± 1.033[ab]	26.56 ± 0.355	40.93 ± 3.945[ab]	32.38 ± 0.871
F (moringa only)	76.21 ± 1.224	86.47 ± 1.595[a]	24.69 ± 0.727	28.04 ± 0.326[a]	32.38 ± 0.727	32.46 ± 0.579

Abbreviations: MCHC, mean cell hemoglobin concentration; MCH, mean cell hemoglobin.
Values are expressed as the mean ± standard error of the mean. [a] Significantly different from the untreated control group at $P < 0.05$; [b] Significantly different from the nicotine control group at $P < 0.05$.
Source: Bamidele et al (14).

the group that was given *Moringa* extract and nicotine concurrently, which showed a statistical reduction in the untreated control group (14). The significant increase observed in the RBC, PCV, Hb, MCV, and MCH of the animal given *Moringa* extract indicates that *Moringa* has a positive hematological effect. The possible mechanism by which *Moringa oleifera* increased the RBC count is linked to the fact that *M. oleifera* is an abundant source of antioxidants (14). It contains some biologically active constituents that should have impacted or increased hematopoietic. It is also evidenced by *M. oleifera* leaf is rich in vitamins A, B, and C. It is one of the best plant sources of minerals, such as iron, and is an outstanding source of protein. The aqueous extract obtained from

Table 5. Results of the effect of ethanolic extract of *Moringa oleifera* leaves on nicotine-induced changes in monocytes, lymphocytes, and platelets levels

Group	Monocytes (%)		Lymphocytes (%)		Platelets ($\times 10^5$)/μL	
	Week 2	Week 4	Week 2	Week 4	Week 2	Week 4
A (untreated control)	3.04 ± 0.161	2.72 ± 0.419	39.26 ± 1.760	35.49 ± 2.894	2.16 ± 0.205[b]	2.58 ± 0.502[b]
B (nicotine control)	1.96 ± 0.377	2.47 ± 0.362	37.24 ± 1.569	38.78 ± 1.193	4.17 ± 0.203[a]	4.23 ± 0.502[a]
C (moringa pre-treatment)	2.50 ± 0.467	2.42 ± 0.361	36.97 ± 0.831	36.85 ± 1.635	2.91 ± 0.215[ab]	3.15 ± 0.750[b]
D (concurrent moringa and nicotine)	2.97 ± 0.655	2.37 ± 0.500	32.32 ± 2.111[a]	36.24 ± 2.502	1.90 ± 0.132[b]	1.90 ± 0.606[b]
E (moringa post-treatment)	2.80 ± 0.400	2.62 ± 0.241	33.79 ± 2.099	37.54 ± 1.798	3.81 ± 0.199[a]	3.15 ± 0.382[b]
F (moringa only)	3.25 ± 0.471	2.83 ± 0.338	37.49 ± 1.604	38.90 ± 2.287	3.18 ± 0.234[ab]	3.24 ± 0.596[b]

Values are expressed as the mean ± standard error of the mean. [a] Significantly different from the untreated control group at $P < 0.05$; [b] Significantly different from the nicotine control group at $P < 0.05$.
Source: Bamidele et al (14).

Moringa oleifera leaves consists of some non-phenolic, bioactive constituents such as glucosinolates, selenium, thiocarbamates, as well as its hydrolysis organic products, namely nitriles glucoraphanin, isothiocyanate and sulforaphane (23). In particular, phenolics like quercetin and kaempferol may work as antioxidants and efficiently scavenge various ROS/free radicals in in-vivo settings.

When compared to the untreated and nicotine control groups, the group that received nicotine and *Moringa* extract concurrently had a statistically lower RBC count. This might be because some aspects of the *Moringa* extract and nicotine interact (14). Compared to the nicotine control group, there was a marked increase in RBC, Hb, PCV, and some other RBC indices in the group treated with nicotine and *Moringa* extract. This demonstrates the effectiveness of *Moringa* in reversing the decrease in these parameters that occurred after the initial nicotine treatment. This suggests that *Moringa* may be beneficial as part of management strategies for former tobacco users. All treated groups, except for the group that administered nicotine and *Moringa* extract simultaneously, showed a marked elevation in platelet levels compared to the untreated standard control. Nicotine may influence platelets by impairing prostacyclin, an antiaggregatory hormone secreted by endothelial cells, by releasing epinephrine, which is known to increase platelet reactivity. Finally, by raising cardiac output and heart, nicotine causes a rise in blood turbulence and may encourage endothelial dysfunction. The increase in platelet count in the group given *Moringa* extract is consistent with the results reported by Hisham and coworkers (24).

Extract of *Haloxylon salicornicum* was also shown to increase nearly all the hematological parameters in the animal except that it caused a decrease in MCV (25). This means that the alkaloid present in the medicinal plant has a beneficial effect in improving the health of the animals.

Ipomea batata ethanol leaf extract was also found to contain moderate alkaloids. When three groups of rats were given three doses for two weeks according to standard protocols, Hct, RBC, Hb concentration, WBC counts, MCHC, and MCV increased significantly compared to the control. The platelet count decreased statistically in all test groups compared to the control group. About the control group, MCV was elevated in all the test groups. Regarding the control group, MCH increased markedly in group 2 but reduced significantly in groups 3 and 4. The rats were reported to be healthy throughout the experiment, with no adverse effects. An increase in RBC count could be linked to the direct stimulatory effect of *I. batata* on hemopoiesis tissues, which include bone marrow and the liver (26).

However, the plant alkaloids in *Carpobrotus edulis* (17), *Maerua crassifolia* (27), *Eugenia jambolana* (28), and *Luffa cylindrica* (29) did not show any hematological effects between different treatment groups in the laboratory animals except for *Luffa cylindrica, in* which WBC and platelets increased at a higher dose (400 mg/kg) following sub-chronic administration. These studies revealed that the plants are safe to use.

Therefore, examination of hematological parameters is particularly beneficial in determining the harmful effects that medicinal plants may induce in animals (17). Hence, the determination of hematological parameters' values is an important diagnostic technique that has a higher propensity to predict the toxicity of therapeutic plants (17).

Benefits, risk, and medical application of the hematological changes caused by alkaloids

Alkaloids are reported to help plants defend themselves against herbivorous animals and pathogens (12) because they contain toxic substances. However, plants containing alkaloids have a great deal of medicinal uses. They could treat diseases such as cancer, malaria, diabetes, cardiac dysfunction, blood clotting-related diseases (12), obesity, and the like. The use of plant alkaloids in managing many diseases has been documented to cause alkaloid toxicity in animals. For instance, pyrrolizidine alkaloid toxicity may ensue secondary to ingesting parent plants for medicinal purposes or via food grain contaminated with the seeds of such plants (30). Animals ' ingestion of plants containing toxic pyrrolizidine is known to cause genotoxic, tetratogenic, hepatotoxic, and tumorigenic effects. In addition, nicotine toxicity could result after ingestion of Nicotiana tabacum leaves, insecticidal products, electronic cigarette refills, cigarettes, and transdermal, as in green tobacco sickness affecting farm workers who harvest tobacco. Severe nicotine poisoning was documented to

result in hypertension, mydriasis, seizure, tachycardia, hyperthermia, fasciculations, respiratory depression, and death (31). Measurement of hematological parameters is essential to determine the changes provoked by the plant alkaloids in response to their toxicity. Changes in hematological parameters caused by nicotine exposure may be a significant cause of a variety of vascular diseases (32). Alteration in platelet aggregation provoked by some plant alkaloids such as rutaecarpine isolated from *Evodia rutaecarpa*, as well as piperine, piperoctadecalidine, piperlongumine, and pipernonaline from *Piper longum L.* results in antiplatelet activity which prevents occlusive thrombus formation (12). Hematological changes may be an index to identify plant alkaloids that are beneficial and safe for the health of the animals. Hence, the assessment of hematological parameters serves as a clinical indicator of animal health and diseases.

Future perspective for application of plant alkaloids provoking hematological changes

Alteration (inhibition) in platelet aggregation by some alkaloids and their medicinal utilization as effective antiplatelet agents may make them screened as candidates for future drug discovery. Some plants with alkaloids that increase hematological parameters may be later considered for developing drugs that can cure anemia and boost immunity. As part of the management or rehabilitative measures for past users of tobacco products, *Moringa Oleifera (*containing alkaloids) may be helpful as it protects against negative hematological changes caused by nicotine.

Conclusion

Plants alkaloids have been known for a wide range of medicinal uses. However, they have both positive and negative benefits for humans and animals. Those that are toxic are reported to have detrimental effects on humans and animals. Alkaloids in plants have been revealed to cause diverse changes in animal hematological parameters. They may cause no change, increase, or decrease in hematological indices. When there is no change in the hematological indices, the plant is safe to use. An increase in the hematological indices due to plant alkaloids suggests that the plant could benefit the animals' health. A decline in the hematological parameters is suggestive of detrimental effects. The changes are linked to the metabolism of the alkaloids and other constituents of the plants.

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Nil.

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