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Spatiotemporal Dynamics of HIV Distribution Pattern and Application of Indigenous Bioresources and Microbicides in Expanding Preventive Options

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1. Introduction

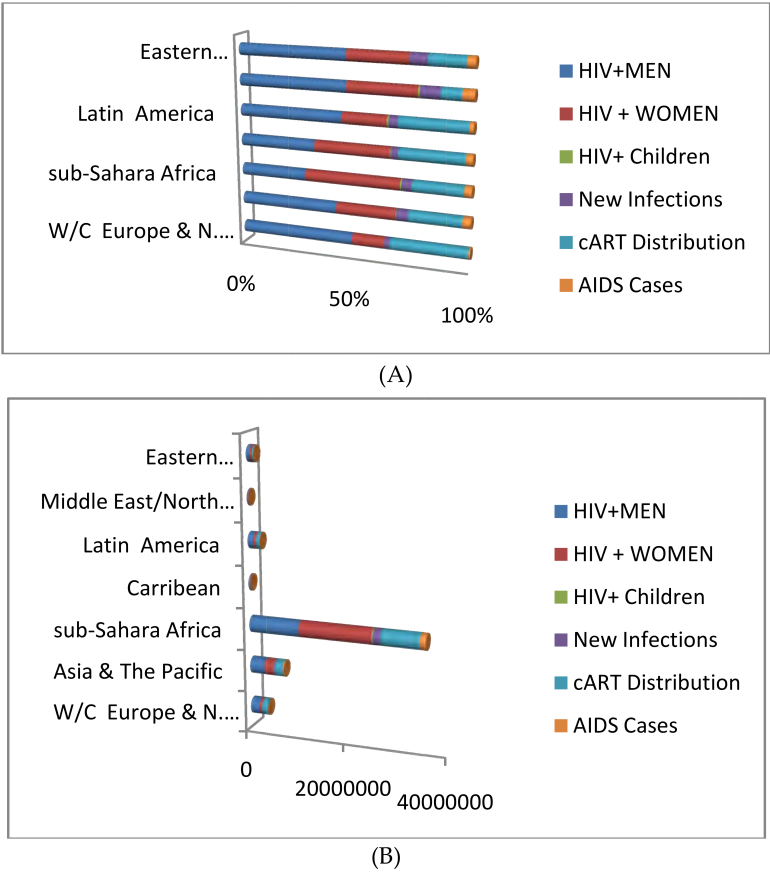
HIV infection has maintained a high number of infections in human population. Currently, there are growing population changes and corresponding challenges including new recombinant circulating forms. The infection is endemic in sub-Saharan Africa with peculiarities in the distribution pattern.

Similarly, distinct transmission models have emanated over the years thus forming a special focal point in the management and prevention of HIV/AIDS. In resource poor settings, management of the disease remains a task as financial, infrastructure, and committed human resources are remarkably low. The current treatment options though widely accepted is still marred with issues of accessibility, resistance, toxicity, and financial burden on the recipient patients. This chapter discusses and brings to concept the current HIV distribution pattern and microbial bioresources deployed as a preventive and treatment option.

2. Global HIV population distribution pattern with emphasis on Africa

The global population of the virus infection has maintained an alarming rate, with record values of more than 34 million people currently living with HIV [1,2] compared to less than 30 million observed in 2002 [3]. The geographical spread of the disease has been astronomical in sub-Saharan Africa, with Nigeria having an estimated amount of 8% of the total global burden of the infection [4].

The distribution and spread of the infection globally is entirely non-uniform and non-homogenous, with more concentrated cases (over 70%) of occurrence observed in Africa alone [5] (Figure 1A/1B and Figure 2). This estimate is extremely significant, given the fact that Africa accommodates approximately 15.3% of the world population [6]. As previously observed in the global spread of the disease, correlation between disease prevalence and social behaviours such as sexual practices and use of intravenous drugs are existential. The spread of infection in Africa is more pronounced and is relative to cultural practices. For example, HIV population is seen to be least prevalent in the northern African countries and the Middle East (Figure 2), which are typically known to practice less of cultural deeds that predispose individuals to HIV infection. Conversely, the spread is dramatically highest in the southern region of the continent [3] where HIV infection appears to have been densely concentrated amongst injection drug users, gays, sex workers, partners of sex workers, etc. [7]. Not only is the prevalence of the disease highest in Africa per global scale, but the rate of rise of occurrence has also been astronomical on the continent, with estimated seven-fold increase in the number of occurrences between 2005 and 2012 [4].



Data presented in Figures 1A and 1B are based on 2014 ECDC report [8], 2014 UN women report [9], and 2014 UN-AIDS Gap report [10]

Figure 1. (A) Regional HIV Population distribution pattern expressed as relative percentage based on 2013 data. (B): Regional HIV Population distribution based on 2013 data.

3. Transmission dynamics models

3.1. Routes of transmission, geographical and racial distribution

In sub-Saharan Africa, the major route of transmission is through heterosexual contact rather than homosexual interaction. In an endemic country like Cameroon, for example, whereas at 2012, the HIV prevalent rate amongst adults was 4.3% (4.0%–4.6%), the infection is concentrated within the 15–49 age bracket in which over 50% of the infected population are women [11]. The major mode of transmission identified by UNAIDS is largely heterosexual, with high occurrence amongst groups such as commercial sex workers, long distance truck drivers, injection drug users, and gay partners [12] with more than half of new HIV infection occurring through heterosexual activity [13]. The transmission of HIV infection is geographic as well as racial (as exemplified by cultural and social values) dependent (Figure 2). Differing factors has been adduced for infection rates in Africans, Asians, Americans, and Europeans which includes social values [14], economic stability/poverty [15, 16], level of awareness [17], and host genetic factors [18].

The three main established routes of transmission of the infection are sexual contact [19], blood transmission [20], needle sharing [21], and vertical (mother-to-child) [22] transmission. Heterosexual transmission seems to be the most common means of infection in Africa with over 60% of the global HIV infections [23] in contrast to other regions of the world, such as in USA which has homosexual transmission and needle sharing as the dominant means [19] (Figure 3). Sharing needles and injection instruments is thought to be three times more likely to transmit HIV than sexual intercourse.

The increased burden of HIV prevalence amongst women in endemic regions have been opined to be due to certain reproductive tract/biological susceptibility [24], social, physical, economical, and even psychological factors which women especially in sub-Saharan Africa are subjected to [25,26].

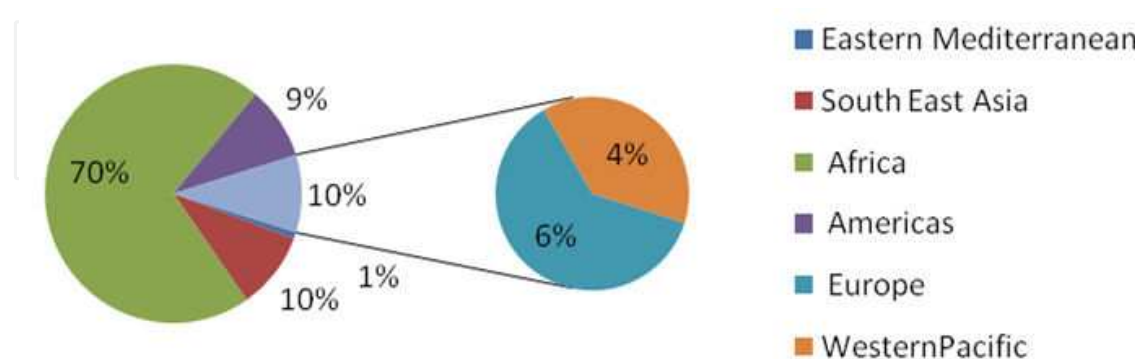
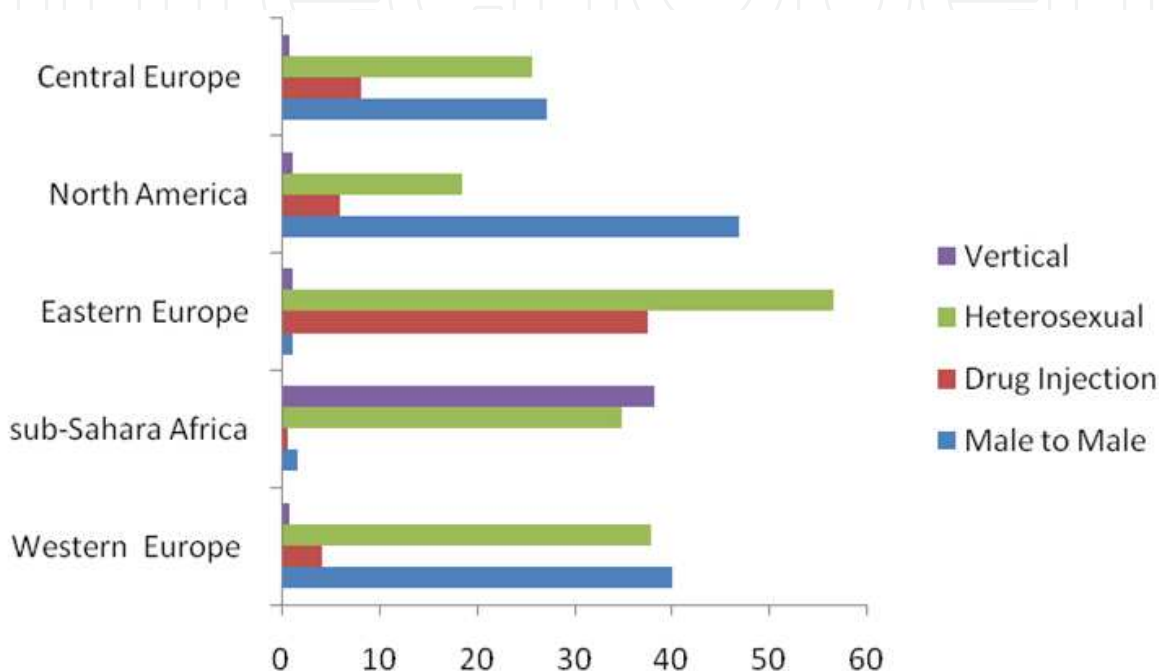


Figure 2. Estimated number of people (all ages) living with HIV based on 2013 WHO data

Available data shows that men who have sex with men (MSM) remain the group with the highest prevalence of HIV infection in the USA, accounting for up to 78% of total infection, as

observed amongst men [27] (Figure 3). The prevalent rates amongst MSM are also recorded to increase in the order, Hispanic MSM (6,700), black MSM (10,600), and white MSC being the highest (11,200) [27]. Up to 16% of total HIV reported cases are due to intravenous drug users (IDUs) in which they represent 8% of new cases [28]. Similarly, Europe has a high number of HIV occurrences from MSM [29]. It could be observed that in high income countries HIV epidemics is highly associated with MEM sexual networks [30, 31,32] while heterosexual contacts prevail in low income regions [33,34,35] (Figure 3).



The data shows the prevalence based on 2013 United Nations Office on Drugs and Crime data from the annual report questionnaire and national Government reports, 2013 UNAIDS report and CDC publications. Note: IDUs stands for injecting drug users.

Figure 3. Regional distribution of HIV routes of transmission in HIV positive population

3.2. Exploring transmission models

Since both heterosexual and homosexual behaviour is a potent factor for increased HIV transmission rate, exploring the dynamics of this mode perhaps could be a sure way of providing and discovering a lasting HIV treatment option and drug design. A number of HIV epidemic models have emerged, particularly the modes of transmission (MOT) model recommended by the Joint United Nations Programme on HIV/AIDS (UNAIDS) [36,37]. The MOT model as developed in 2002 aims to identify persons at risk of HIV infection [38] with subsequent prevention policies and programmes [39]. This model was recommended for country-wide studies in the year 2008 as part of a synthesis process supported by UNAIDS and the World Bank Global HIV/AIDS Monitoring and Evaluation Team [40], with emphasis on local content and immediate environment prevailing circumstances. The MOT model

utilizes accurate information on recent prevalence of HIV infections in a given population and the assumed patterns of risk behaviour within different risk groups (MSM, prostitutes, etc.) to calculate the expected distribution of new adult HIV infections the next year in terms of the mode of exposure. Certain considerations are necessary for a comprehensive and adequate utilization of this model either at country or community level studies. These considerations as noted by WHO are the proportion of the adult male and female population that belongs to each of several risk groups identified, such as commercial sex workers and their patronizers, injection drug users, men who sex men (MSM), persons of multiple heterosexual sex partners, the low risk group such as partners of persons with higher-risk behaviour and married or cohabiting couples with one monogamous heterosexual partner in the last year [41]. The model tends to resolve issues such as complexity in risk groups, for example, a prostitute who is a drug injection user. Secondly, the prevalent rate of HIV infection and of a generic sexually transmitted disease (STI) identified in each risk group [41]. Thirdly, the average numbers of sexual or injecting partners and exposures per partner with considerations of personal level protective behaviour (such as condom use or the use of new needles), for individuals in each risk group and lastly the probability of HIV transmission per exposure act in each risk group, taking into account the effect of STIs and the prevalence of male circumcision [41].

4. Recombinant circulating forms and distribution pattern

The capacity of HIV to exhibit a unique high genetic variability has posed a major challenge to its treatment [42]. The genetic diversity is also attributed to a high error rate of the HIV genome during transcriptase reaction and also high genetic recombination rate [43].

Recombination is defined as the process whereby various subtypes or strains of the HIV shuffle their genomic characteristics to form an entirely new strain. This recombination tactic, a system of alteration of the HIV genetic constitution, is mostly common with the HIV subtype-1 (HIV-1) and it is commonly called new circulating recombinant forms (CRFs) (Table 1). There also exists the HIV subtype-2 (HIV-2), which is relatively less pathogenic in comparison to HIV-1 [44]. The occurrence of CRF is closely linked to the dynamism of the HIV infection and epidemic and obviously to failure of most specific therapeutic target in eliminating the virus [45-47]. The study of the distribution pattern of the various subtypes is therefore highly crucial for effective HIV management especially in endemic regions of the world. Recombination occurs at a very rapid rate estimated to be in the order of 2.8 cross-over per genome per cycle [48]. Recombination events between subtypes lead not only to an ever increasing diversity of the HIV strains [49] but also presents astonishing scenarios of emerging strains with resistance to the common antiviral drugs [50,51]. The numbers of CRFs are increasing astronomically global, partly because of the emergence of recombinants of the various subtypes in various local epidemiological regions [46]. There has also been a correlation between the emergence of divergent subtypes in a population and the teeming occurrence of disease cases. For example, in Cameroon, the number of newly infected individuals increased from 8,596 to 10,625 between 2006 and 2007 as the number of recombinant subtypes increases in the studied population [47]. Criteria set to define a new subtype, sub-subtype, or CRF include having the representative

strain identified in at least three individuals who have no direct epidemiological relationship. Three full-length genomic sequences are required but two complete genomes together with partial sequences of a third strain could also define a new subtype, sub-subtype, or CRF. CRFs are derived from recombination between viruses of different subtypes which are each given a number. CRF12_BF, for example, is a recombination between subtypes B and F.

HIV type	GROUP (%)	SUBTYPE(sub-subtype)	CRFs	GEOGRAPHICAL SPREAD
I	M: Major (90%)	A(A ₁ ,A ₂ ,A ₃)	CRF19_CPX,CRF01_AE,CFR14_BG,CRF03_AB,31_BC,CFR06/18_CPX	West Africa ,Cuba[52,53,54]
		B	CRF07/8_BC,CRF15/48/51/52/53/54/55/58/59_01B	Europe, Japan, Thailand, Australia, the Americas [55]
		C	CRF10/41_CD,CRF11/45/49/37/36_CPX	S/E Africa, India, Nepal, China [55]
		D	CRF05_DF,CRF13_CPX,CRF16_A2D,CRF19_CPX	Eastern and Central Africa [55]
		E	CRF01_AE*	Africa [55]
		F (F ₁ F ₂)	CRF12_BF1,CRF22_01A1,CRF25_CPX,CRF26_AU	Central Africa, S. America, Eastern Europe [56]
		G	CRF02_AG,CRF09/56/65_CPX,CRF20/23/24_BG	Africa and Central Europe [56]
		H	CRF32_06A1,CRF33/34_01B,CRF35_AD,CRF38/39/40/42/44/46/47/70/71/72_BF,CRF43_02G	Central Africa [56]
		I	CRF04_CPX	Only in central America [57]
		J	CRF50_A1D,CRF60/61/62/64_BC,CRF17_BF1CRF49_01B,CRF63_02A1	North, Central and W. Africa Caribbean [56]
		K	CRF04/06/18/27_CPX,CRF21_A2D	Congo DR and Cameroon [56]
II	N:Non- M,Non-O			
	O:Outlier			Cameroon [58]
	P:Pending			West-Central Africa, Cameroon [59]
	A			None

HIV type	GROUP (%)	SUBTYPE(sub-subtype)	CRFs	GEOGRAPHICAL SPREAD
	B			W. Africa, Angola, Mozambique, India, Brazil[60]
	C-H			West Africa [61,62] Liberia, Sierra Leone, Ivory Coast [61,62]
* Recombine only with A, G, H, K, U, CPX=complex recombination of several subtypes (ADG)				

Table 1. HIV Classification and global CRFs

5. HIV/AIDS prevention strategies, how well have they worked?

There are three major strategies of HIV prevention, namely, education or knowledge base, contraceptives, and antiretroviral treatment.

5.1. Peer education

Amongst the many ways of curbing the onslaught of the HIV, one of the most vital is educating the populace about the disease and its transmission dynamics. This significantly prevents re-infection and protects those who are not already infected [63, 64, 65]. Therefore, inadequate knowledge of the disease transmission equals resultant failure of all the measures originally put together to tackle the spread of the disease. In a research conducted in 2006 to access the effect of prior knowledge of HIV transmission relative to the number of occurrence of the infection in Boston, USA, it was found that a significant proportion of the infected people are those with significantly little or no knowledge of the disease or its mode of transmission [66]. Increase in HIV education, particularly amongst young people, remains the most effective way of tackling the HIV onslaught. Where this form of education is limited, the disease is known to prevail [67, 68] as also noted from various data in sub-Saharan Africa. Education on HIV/AIDS plays a major role in controlling the spread of the disease amongst young people, which consequently determines the global spread of infection. HIV infection has been captured as the second most prevalent killer amongst young people. As of 2012, one-third of the global new HIV infection was discovered to be amongst young people, with total infection of about 780,000 and concentrated within 15–24 age group [69]. This number has obviously dropped down from 2012 to present due to vigorous and continuous education campaigns but, even so, HIV/AIDS deaths amongst the young people worldwide are still at an alarming rate [70, 71]. Proper education enables young people and married adults to better protect themselves against the sexually transmitted route of HIV infection, vertical transmission, and also behaviours such as intravenous drug use [72]. So significant was the global implication of HIV/AIDS infection on young people that it was opined that HIV education should be dispensed even to healthy ones.

5.2. Antiretroviral prophylaxis

In poor-resource settings, it is not uncommon to use antiviral therapy as a means of controlling the spread of infection. Experiments however showed that the administration of antiviral therapy, although it has a considerable control rate on HIV infection, is limited in its cost. Many HIV populations do not have access to ART [73] and to others are very expensive [74]. In Nigeria for instance the price of generic ART reported in 2001 could be over 10 times more expensive in comparison with Asian countries and about 79% lower in some European countries [75]. When antiviral therapy is considered as a chosen measure for HIV treatment, an additional use of these therapeutic agents serves as a preventive measure rather than a treatment option. The application of ART at a specific stage of disease progression (measured by computerised simulation incorporating CD4 count and HIV RNA level) has proved to be cost effective [76]. HIV prophylaxis treatment refers to the institution of measures taken to protect a person from HIV infection to which the individual has been anticipated or is liable to be exposed to HIV. HIV prophylaxis could either be post or pre-treatment option based. According to the US CDC, pre-exposure prophylaxis (PrEP) is designed for individuals who do not have HIV but who are at substantial risk of getting it to prevent HIV infection by taking an antiretroviral drug every day [77]. Truvada which contains two HIV drugs (tenofovir and emtricitabine) is usually prescribed [78]. On exposure to HIV through sex or injection drug use, these drugs can work to keep the virus from establishing a permanent infection. PrEP has been shown to reduce the risk of HIV infection in people who are at high risk by up to 92% when adhered to for at least 3 months [77]. Similarly, WHO describes post-exposure prophylaxis (PEP) as contrasted by PrEP as a short-term antiretroviral treatment to reduce the likelihood of HIV infection after potential exposure, either occupationally or through sexual intercourse [79,80]. Post-exposure prophylaxis (PEP) involves taking a 28-day course of ARVs, for adults Tenofovir combined with either lamivudine (3TC) or emtricitabine (FTC) is prescribed. The recommended third drug by WHO is ritonavir-boosted lopinavir (LPV/r), which is also a preferred drug for HIV treatment. Zidovudine (AZT) and lamivudine (3TC) backbone drugs are used for children aged 10 or below, with ritonavir-boosted lopinavir (LPV/r) recommended as the third drug choice [81-84]. As effective as this preventive option may be, it faces challenges of adherences which has reduced its efficacy to less than 56%. Another challenge is the accessibility of the drug to individuals and accurate timing of exposure.

Limited studies on supply and distribution of antiviral drugs in poor-resource areas indicated that the mechanisms of supply and delivery of these drugs are not cost-effective [85-87]. The most significant concern is rural population having access to HIV antiviral drugs and the availability of laboratory facilities to monitor viral loads of patients on antiviral drug as response to therapy and for full HIV clinical management. One of the standard laboratory interventions used in the developed countries to monitor patients receiving antiviral drugs is the plasma viral load monitoring assay [88] which is not readily accessible to the wider population of HIV patients in resource-poor regions [89].

5.3. Contraceptives

Contraceptives may simply be understood as devices or pills used to prevent unwanted pregnancies and diseases mostly sexually transmitted. These can be in the form of drugs,

hormones, or devices such as condoms and intrauterine devices (IUD). Evidently, hormonal contraceptives and pills do not protect against HIV or other sexually transmitted infections (STI). At present there are no contraceptives, with the exception of condoms (male and female), that protect against HIV infection [90]. Since the only forms of birth control that will protect against HIV are abstaining from vaginal (and anal) sex or using condoms while having sex, WHO therefore recommends dual protection technique for unwanted pregnancy and HIV prevention [91]. Birth control options that do not protect against HIV infection include oral contraceptives, birth control shot (injection of the hormone Depot Medroxyprogesterone Acetate (*DMPA*) in the arm to release progestin)/Depo-provera, morning after pill (Levonorgestrel or Ulipristal acetate) used after sexual activity, implants (implanon/norplant), IUDs which release progestin, female condoms such as diaphragm/vagina ring/sponge/cervical cap, withdrawal and spermicides. Currently, a new intravaginal ring that helps prevent pregnancy while simultaneously releasing low doses of an antiretroviral drug that reduces a woman's risk of contracting both HIV and genital herpes has been designed [92,93]. This device releases doses of the contraceptive Levonorgestrel and the antiretroviral HIV medication tenofovir after being inserted in the vagina for 90 days and has demonstrated a 39% protection against HIV infection in women [93]. It is obvious that many contraceptive pills may not be compatible with ARTs, the widely prescribed antiretroviral drug efavirenz substantially reduces levels of the hormonal contraceptive Levonorgestrel [94] and increases the risk of HIV infection [95,96].

6. Development of bioresources for HIV management

Bioresources relate to the total biological variation manifested in individual plants, animals, or their genes, which could be utilized by humans for beneficial use such as drugs, food, livestock feed, etc. It also refers to the development of improved crops and animals for higher yield and tolerance to biotic and abiotic stresses. However, despite the global investment in bioresources and machinery to curb the spread of HIV, weak health systems and inadequate human resources are continuing to be major barriers to the elimination of the disease [5]. There is therefore need for an upgrade of the existing methods of disease control and prevention to include local biological resources such as herbs and other plant materials. Several biological organisms mostly plant species have been employed in preventing and managing HIV infection in developing or resource poor countries. Recently, this has metamorphosed into an institutional traditional medicine sector with growing patronage and herbal formulations. Though active antiretroviral therapy (ART) is the principal method for preventing immune deterioration, about 80% estimated Africans still use herbal remedies [97]. In addition, prophylaxis for specific opportunistic infections is indicated in particular cases. There has been increased use of local resources in the treatment of HIV/AIDS known as alternative or complementary therapy [98] with growing scientific journals that publish its procedure and outcome. Some herbal remedies have been found to inhibit one or more steps of HIV replication (Table 2). Though most herbal preparations treat HIV opportunistic infection [99], many research groups are exploring the biodiversity of the plant kingdom to find new and better anti-HIV drugs with novel mechanisms of action. Since some plant substances are known to

modulate several cellular factors, such as NF-kappa B and TNF-alpha, which are also involved in the replication of HIV. Their role as potential anti-HIV products should therefore be a desirable focus of attention. In conclusion, several plant-derived antiviral agents are good candidates for further studies, with a view to exploring their potentials and application in systemic therapy and/or prophylaxis of HIV infections and most probably in combination with other anti-HIV drugs. Plant resources in the form of herbal preparations provide cheaper and accessible antiretroviral therapy to the poor populations.

6.1. Selected plant resources with anti-HIV activity

Plant	Identified Compound	Mechanism
Daphne acutiloba (Rehder Thymelaeaceae)	Wikstroelide M	Inhibition of HIV1/2 reverse transcriptase activity and integrase nuclear translocation through disrupting the interaction between integrase and LEDGF/p75 [100]
Dracontium peruvianum (jergón sachá)	D-tubocurarine and Phytochemicals	Possibly as a protease inhibitor [101]
Croton tiglium	Phorbol esters	Inhibitory effects on HIV-1 proliferation and its protease [102]
Mangosteen	Mangostin and gamma-mangostin	Inhibitory activity against HIV-1 protease [103]
Licorice	Glycyrrhizin	Inhibits HIV replication [104,105]
Andrographis paniculata	Diterpene lactones: (andrographolide)	Inhibit cell-to-cell transmission, viral replication and syncytia formation in HIV-infected cells [106]
Acer okamotoanum	Flavonoid gallate ester	Anti-HIV-1 integrase Activity [107]
Rhus succedanea L. Garcinia multiflora	Biflavonoids, robustaflavone, and Hinokiflavone	Inhibits HIV-1 reverse Transcriptase [108]
Ancistrocladaceae Ancistrocladus korupensis	Michellamines A and B	Inhibits reverse transcriptase, cellular fusion, and syncytium formation [109]
Annonaceae Polyalthia suberosa	Lanostane-type triterpene, suberosol	Anti-HIV replication activity [110]
Apiaceae Lomatium suksdorfii	Suksdorfins	Suppresses HIV-1 viral Replication [111]
Asteraceae Achyrocline satureioides (Lam.) DC (Marcela);	Dicaffeoylquinic acids: 3,5-dicaffeoylquinic acid, and 1-methoxyoxalyl-3,5-dicaffeoylquinic acid, Wedelolactone, a coumarin derivative;	Irreversible inhibition of HIV-1 integrase [112]
Arctium lappa (Burdock)	Orobol (an isoflavone derivative)	Inhibits HIV-1 replication;

Plant	Identified Compound	Mechanism
		blocks cell-to-cell transmission of HIV-1 [113]
Combretaceae Combretum molle R.Br. ex G.Don	Gallotannin	Inhibits HIV-1 reverse transcriptase [114]
Terminalia chebula, Euphorbia pekinensis	Gallic acid and galloyl glucose	Inhibits HIV reverse transcriptase and integrase [115]

Table 2. Selected plant resources with antiviral activity

6.2. Challenges of HIV Bioresources Development and Bioprospecting in Developing Nations

Several challenges face development of bioresources effective in enhancing antiretroviral development in low and mid-income countries. Such problems are mostly institutional highlighted as follows:

1. Lack of appropriate framework for deployment and exchange of bioresources materials within and amongst countries
2. Weak genetic banking infrastructure
3. Absence of advanced analytical and simulation laboratories
4. Weak linkage of existing bioresources centres to local industries
5. Absence of effective communication channel to supposed end users/beneficiaries of the eventual product
6. Weak standardization and evaluation procedure for products emanating from bioresources
7. Absence of a bioprospecting policy

7. Microbicides as preventive/treatment options

Microbicides are applications applied inside the vagina or rectum that protects against sexually transmitted infections (STIs) including HIV. These types of chemical applications could be formulated as gels, creams, films, or suppositories. Microbicides are potential HIV prevention options which can reduce the spread of HIV especially among women in developing countries. Without a preventive HIV vaccine, microbicides [116] offer an alternative to condoms as the most feasible method for primary prevention of HIV. Microbicides- intravaginal/intrarectal topical formulations of anti-HIV agents have also been proposed to prevent HIV transmission. Currently, antiretroviral-based microbicides have been achieved for the prevention of HIV new infections among women after many years of failed trial. More than 60 candidate agents have been identified to have *in vitro* activity against HIV, several of which have advanced to clinical testing stage.

At least 10 reverse transcriptase inhibitors and 16 entry inhibitors have been or are in the process of being investigated in clinical or preclinical trials. Ideally, these compounds are characterized by high potency, low absorption from the vagina to the blood to minimize development of resistance, and have a long half-life in order to remain active over a long period. Tenofovir has also been formulated as a topical vaginally applied gel and assessed for its protective effect against Simian immunodeficiency virus (SIV) in macaques. The results indicated that the macaques receiving the tenofovir gel were completely protected from infection [117] and in human trials [118]. The results of the human trial were released in July 2010 and showed that use of the gel reduced acquisition of HIV infection by 39% overall, and by 54% in women who were highly adherent to gel use [118].

Topical microbicides are grouped into five classes of agents, based on their mode and site of action [119] (Table 3)

Microbicides type	Mechanism	Formulation and year	Countries of clinical trial
Surfactants/membrane disruptors-based microbicides	Virucidal action through disrupting the viral envelope	1. Nonoxynol-9 (N9) 1985 [120] 2. C31G (cetylbetaine and myristamine oxide) 1997 [121] 3. Sodium lauryl sulphate (Invisible Condom) 2002 [122]	Kenya, Cameroon Ghana,
Vaginal milieu protector based microbicides	Enhance the natural protective mechanisms within the vaginal canal through altered pH range	BufferGel, PRO 2000 Gel [123]	Malawi; South Africa; Hlabisa, South Africa; Zambia; Zimbabwe; USA
Microbicide based on inhibition of HIV entry in the host cell	Negative charge, anionic polymers interact with HIV's viral envelope proteins and interfere with the attachment and fusion of HIV to target cell	CMPD167, Maraviroc (MVC), cyanovirin-N, Cellulose sulphate, SPL7013.2010 [124,125]	USA, Kenya Benin, India, Uganda, South Africa
Microbicides that act after entry of HIV in the host cells	Prevention of replication and release through inhibition of the virus-encoded reverse transcriptase (RT) or integrase (IN)	Tenofovir 2010 [126-128]	South Africa, Uganda, Zimbabwe
Microbicides based on inhibitors with unknown mechanism of action	Combination of extracts prepared from plants with anti-retroviral properties of unknown mechanism	Praneem 2005 [129] Basant	India

Table 3. Microbicides and their mechanism of action

For development of acceptable microbicide, researchers must develop not only the active ingredient but also a socially acceptable, affordable, and easy to apply microbicide providing protection for several days and/or weeks. Other major issues include how a microbicide might affect sperm and the possibility of causing adverse effects in women reproductive health. In Table 3 the listed microbicides failed to achieve the desired results except for tenofovir gel which showed 39% less likelihood for users to become infected with HIV than women who received a placebo gel. For women who adhered to tenofovir gel prescription correctly, HIV infection was 54% less likely than the placebo group.

8. Conclusion

HIV is widely distributed globally. Strong effort and interpersonal encouragement should be channeled on exploring and developing bioresources with antiretroviral potential to serve as a springboard for cheaper and locally available HIV drugs in addition to developing appropriate bioprospecting policies. Behavioural change and abstinence remain a sure means of HIV prevention, but need to be complemented with additional biomedical options especially in the populations most vulnerable to HIV infection.

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