An overview of pharmacological activities of acridine derivatives

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ABSTRACT

The derivatives of acridine can be served as a lead molecule of an antibacterial, anti-viral antiprotozoal, anti-viral, antitubercular, anti-fungal, anti-malarial and anti-cancer agents. Even though the usage of acridine becomes limited due to its side effects, so many potent and safe compounds can be derived through molecular modification in the acridine ring. Since the resistance of pathogens and tumour cells has become more common nowadays, it necessitates the search of new drug candidates. Since the treatment and management of Alzheimer’s disease is such a complicated and proper drug regimen is not designed so far, The cholinesterase activity of acridines can be used to derive novel compounds from treating Alzheimer’s disease. The mosquito larvicidal activity of acridines is considered as an advantage as vector control to reduce the spreading rate of malaria. Unfortunately, the versatility of the acridine molecule is not entirely explored still. If new approaches may overcome the drawbacks of the acridines such as resistance of pathogens and tumour cells in synthesis and formulation acridine analogues will become a useful drug candidate for the treatment of diseases mentioned above. So this article aims to seek the attention of researchers in the acridine to utilise it’s a wide range of biological activities in the development of novel drug molecules for the various diseases in the future.

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INTRODUCTION

Acridine (Figure 1) is a versatile heterocyclic nucleus. It was discovered and announced by Graebe and caro in 1870 (Acheson, 1973). Acridine was identified as a new basic material in the anthracene fraction of coal tar. Due to it’s acrid smell and irritating action on the skin and mucous membrane it was named as acridine subsequently, the different kinds of nomenclature and numbering systems are used (Acheson, 1973). Heterocycle fused acridine possess a variety of biological activities including Ca²⁺ releasing, anti-viral, anti-microbial and antitumour properties. Acridine derivatives also act as an enzyme inhibitor and have DNA intercalation and chelating metal properties (Water and Munawar, 1998). When we are looking back history so many acridine derivatives were utilised for various medicinal purposes in different periods. So many novel drug molecules have been developed by

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modification of the acridine nucleus. The molecular modification provides so many potent molecules from acridine; for example, bistacrine analogues proved an excellent anti-Alzheimer activity than parent anti-Alzheimer drug tacrine, Acridinones and carboxylates of acridine showed an excellent mosquito larvicidal activity. Analogues of 9-anilino and benzoyl styrene exhibited anti-malarial activity. Braco-19 is a trisubstituted acridine derivative proved a significant anti-viral and anti-cancer activity. Benztriazolo acridine derivative showed remarkable antibacterial activity. Derivatives of 9-substituted acridines and polycyclic acridines have significant antitubercular activity. Imidaza and thiaza acridine derivatives showed an optimum anti-cancer activity. When thiazolidinedione connected with an ethacridine molecule, it will become a potent anti-fungal agent. Compounds of 9-anilino acridines and acridinones are considered as potent antileishmanial agents. In this review, we are aimed to discuss the synthesis and evaluation of respective biological activities of those derivatives of acridines.

**Mosquito Larvicidal Activity of Acridine Derivatives**

A series of acridinone related compounds were synthesised and characterised by spectral studies then evaluated against the larvae A.aegypti and C.quinquifasciatus. In which the synthesised products were diluted with dechlorinated water and made the solution 2% by Dimethyl sulfoxide. In the larvicidal bioassay five sets container with 20 numbers larvas of same species mixed with 249 ml of dechlorinated water and 1 ml of test solutions at desired concentrations. Water and dimethyl sulfoxide were taken as a negative control. The number of died larvae was counted after 24 hrs. The same procedure performed in triplicate and the average value considered. The compounds 5a (Figure 2) and 3b (Figure 3) showed excellent activity against A.aegypti and C.quinquifasciatus respectively (Roopan et al., 2017).

In this study, E-2-benzylidine-7-chloro-9-phenyl-3,4-di hydro acridine-1(2H)-ones synthesised and characterised by FTIR, \(^1\)H and \(^{13}\)C NMR and ESI-MS spectra. Screened for their larvicidal activity against anopheles stephensi and Hippobosca maculate. Most of the compounds showed good activity against both the larvas (Bharathi et al., 2015).

**Anti Malarial Activity of Acridine Derivatives**

The anti-malarial activity of 9-anilino acridines evaluated by means of targeting an enzyme topoisomerase-II and \(\beta\)-Haematin in malarial parasites.3,6–Di amino substitution in acridine ring showed considerable improvement in the parasiticidal activity against plasmodium falciparum. Most of the compounds showed remarkable inhibition of \(\beta\) haematin formation. It was thought to be the presence of N, N di methyl amino group in anilino

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Table 1: Zone of inhibition (Diameter in mm)

| Compound | E.Coli | B.Subtilis | A.Niger | C.Albicans |
|----------|--------|------------|---------|------------|
| 1        | 21     | 16         | 14      | 26         |
| 2        | 17     | 21         | 4       | 15         |
| 3        | 13     | 2          | 6       | 8          |
| 4        | 22     | 19         | 17      | 10         |
| 5        | 21     | 13         | 16      | 5          |
| Standard | 08     | 4          | 9       | 6          |
| Control  | 0      | 0          | 0       | 0          |

Table 2: Functional groups of synthesised compounds 5 a, c, g and m

|        | R1 | R2 | R3     | R4 | R5     |
|--------|----|----|--------|----|--------|
| 5a     | H  | H  | NO2    | H  | H      |
| 5c     | H  | H  | H      | H  | NO2    |
| 5g     | CH3| H  | H      | H  | NO2    |
| 5m     | H  | CH3| H      | H  | H      |

Figure 3: Compound 3b

Figure 4: Compound-14

Figure 5: Compound K4

ring advantageous to this activity. In this study, one another fact was found that the presence of 3,6-dichloro analogues are potentiated the β haematin inhibitory effect of acridines than 3,6 – di amino and the mono chloro substituted analogues. It was evidenced by the compound 13 (Figure 4) proved a maximum activity among others. Those studies opened up the possibility of development of novel 9-Anilino acridines to inhibit the topoisomerase-II and β-Haematin formation to mitigate the resistance of malarial parasites towards the conventional anti-malarial agents (Saranya et al., 2003). Condensation reaction carried out between quinolone and acridine scaffolds to synthesise Acridine-Quinoline hybrids and performed the molecular docking studies with the binding site of PdHFR-TS enzyme with the aid of Glide V5.6.5 best compounds selected from docking studies to carry out the In vitro evaluation of anti malarial activity against resistant strains of plasmodium falciparum by micro dilution technique. Compound K₃ (Figure 5) was proved an effective therapeutic agent than standard drugs such as quinine and chloroquine (Kalpna et al., 2016).
Anti-viral Activity of Acridine Derivatives

The anti-HIV activity was observed with BRACO-19, a trisubstituted acridine derivative. An anti-HIV activity may be due to its ability to bind with dynamic G-quadruplex region of DNA. Inhibition of promoter activity and anti-viral effects have been observed when BRACO-19 stabilised this region. The anti-viral mechanism of action of BRACO-19 was characterised by analysing its activity towards a broad range of HIV-1 strains, host cells and infection modes. Nevirapine used as standard. Anti-viral assays were carried out in HIV-1 infected MT-4 –LTR –eGFP and MTT based anti viral assay in...
HIV infected MT-4 cell line. In the first method, RPMI 1640 medium supplemented with 10% fetal bovine serum, 0.1% sodium bicarbonate, 20 μg/ml gentamycin.

MT-4-LTR-eGFP is infected with HIV-I(IIIb) at a multiplicity of infection of 0.5 and incubated at 37°C after an hour the cells were washed and seeded in the presence of serial dilutions of BRACO-19 in a 96 well plate. Flow cytometric analysis was performed to determine the eGFP expression to measure HIV-1 production. The second method was performed by tetrazolium-based colorimetric assay. In which MT-4 cells were seeded in the HIV-I(IIIb) virus stock at 100-300 CCID50 in the presence of serial dilutions of BRACO-19. Cell viability measured five days after infection. Sample absorbance was measured in two wavelengths (540 and 690 nm) and the median absorbance of 3 wells was calculated, anti viral assay performed in HIV-I infected peripheral blood mono nuclear cells. In which the concentration required to produce 50% inhibition of HIV-1 infection—viral binding assay performed by incubation of stock dilution of HIV-I cells with a serial dilution of BRACO-19. The amount of P24 antigen was measured. Virucidal assay performed by HIV-I incubated with various concentrations of BRACO-19 and the viral infectivity was measured after five days. It was the first time the anti viral activity of BRACO-19 evaluated through G-Quadruplex mediated mechanism of action (Perrone et al., 2014).

Guanine rich quadruplexes are targeted by Braco-19 for its anti viral activity against HSV. HSV-1 genome shows multiple clusters of repeated sequences that form very stable G quadruplexes. Virus production was inhibited by the treatment with G quadruplex ligand Braco-19 and the intra cellular DNA in infected cells was decreased. Braco-19 exhibited a significant anti viral activity at 1μm, and the activity increased up to 70% at 25 μm. This work suggests the G quadruplex ligands may be considered as a new target for the treatment of herpetic infections (Artusi et al., 2015).

Antibacterial Activity of Acridine Derivatives

In this study, benzotriazole substituted acridine analogues were synthesised and investigated the antibacterial activity. The 9-substituted acridine derivatives were synthesised by the reaction between 9-Chloro acridines with 0-phenylene diamine. Those compounds were finally condensed with benzotriazole to form benzotriazole substituted acridine derivatives. The reaction was monitored by TLC plates using chloroform: methanol (9:1) confirmed by visualisation of spots by iodine vapours. The synthesised compounds were characterised by IR and 1H NMR spectral studies. The antibacterial activities of synthesised compounds investigated against gram-positive (S.aureas and B.subtilis) and gram-negative (E.coli) bacterial strains by cup plate method. The synthesised compounds were diluted at the concentrations of 100,500,1000,5000,10000 g ml\(^{-1}\). Standard drug (Ampicillin) is diluted to 100 μg ml\(^{-1}\). Previoulsy inoculated suspension carefully poured into the Petri dishes containing medium. The uniform quantity of the test solutions and standard solution were applied carefully on the surface of the solid medium in cavities prepared in agar, incubated for about 18 hours at 32-35°C. Zone of inhibition was accurately measured. The benzotriazole substituted compounds shown significant anti bacterial activity compared with standard drug ampicillin. It was cleared from the results of the benzotriazole substitution at 9\(^{th}\) position of acridine will give rise to potent antibacterial agents (Singh et al., 2011).

Rivanol is a substituted di amino acridine it has been already used to induce abortion in the mid-trimester, and it was also found that rivanol can bind intensely to DNA eventually leads to the development of mutation. In this study, rivanol is screened for bacterial mutagenic activity against
E.coli K12 Strains which has the genetic markers supF,supE,gal and hsdR. Luria broth culture used to inoculate the strains and rivanol was added at different concentrations and incubated at 37°C to stationary phase. A uniform inoculum about 10^7 cells/ml. The concentrations of viable cells were determined by plating dilutions of each culture of Luria broth agar, and plating dilutions of each culture determined the concentrations of up mutants on minimal glucose-containing agar. Rivanol treated samples had fewer

Viable cells than untreated controls. Rivanol did not increase the frequency of upp mutants at the concentrations below 100μg/ml, but the mutant frequency was increased up to 8 fold at the Concentrations 100μg/ml. It shows that rivanol exhibits dose-dependent mutagenic activity. Rivanol bound to bacterial DNA 2-5 times greater than acridine orange and proflavine. It reveals that the selective bacterial toxicity achieved when the acridine nucleus is 6,9-di amino-substituted analogue (Miriyam and C, 1983).

**Anti Tubercular Activity of Acridine Derivatives**

Several analogues of 2-methoxy-9-Substituted acridine and 6-chloro-2-methoxy-9-substituted acridine were synthesised. In which the chlorobenzonic acid was treated with methoxy aniline in the presence of K2CO3/Cu/DMF and the resultant compound was react with pocl3 led to the formation of substituted chloro methoxy acridine, which was again reacted with sulphanalimide and 4-amino acetophenone and produced the derivatives of the same. The synthesised compounds were screened for their anti tubercular activity by microplate alamar blue assay method against M. Tuberculosis H37 Rv and Rifampicin was used as positive drug control. It was concluded that the introduction of chlorine atom brings a significant contribution to acridine analogues to exhibit the optimum anti-tubercular activity (Aly and Abadi, 2004). The synthesis of twelve acridine and polycyclic acridine molecules carried out by Friedlander reaction mechanism. In which one-pot reactions conducted between 2-amino-5-chloro or 5-nitro benzophenones and a variety of cyclanones and indanones in the microwave oven. The synthesised products are subjected to the evaluation of antitubercular activity against M.Tuberculosis H 37 Rv. Among the synthesised compounds cycloptenta acridine derivatives proved an antitubercular activity almost similar to that of rifampin. Those molecules might be lead molecules in future (Muscia et al, 2014).

**Anti-Fungal Activity of Acridine Derivatives**

A series of 9-substituted acridine derivatives were synthesised by the reaction between di phenylamine in ethanol and carboxylic acid at 150°C for 3 hours. The completion of the reaction is confirmed by Thin layer chromatography, and the reaction mixture is extracted with ethyl acetate. Totally five compounds were synthesised, i.e. acridine -9-amine (1), 9-methyl acridine (2), 9-propyl acridine (3), 9-(4-nitro phenyl) acridine (4), 9-phenyl acridine (5). The evaporation of the organic layer obtains products.

Synthesised compounds purified by column chromatography by using an eluent ethyl acetate and cyclohexane (2:8). 1H NMR and IR spectroscopy characterise the synthesised compounds. The synthesised compounds were investigated their anti fungal activity against Calibicans &A. Niger and anti bacterial activity against B.subtilis and E.coli by the cup-plate method. DMSO is used as control and Ampicillin(100μg/ml) & ketoconazole(100μg/ml) used as standards for anti-bacterial and anti-fungal activities, respectively. MIC values are calculated after the incubation of 24 hours and 48 hours for bacteria and fungi respectively and given in the Table 1 (Ranganath, 2017).

New anti microbial compounds containing more than one pharmacophore were synthesised. In this experiment, an already established acridine molecule ethacridine was connected with 2-amino substituted thiazolidinones and the pharmacophoric amino or aldehyde groups created by an appropriate synthetic scheme. The synthesised compounds are characterized by IR and NMR spectroscopy and studied their antibacterial and anti-fungal activities. Antibacterial and anti-fungal susceptibility tests were performed in vitro with standard bacterial cultures of S.Aureas, E.coli, K.Pneumoniae, B.subtilis, and standard fungal cultures of Calibicans, C.Glabrata, C.Krusei, C.Kefyr, C.tropicalis, C.Parapsilosis respectively by serial broth dilution technique. The experimental results showed that the synthesised compounds exhibit bacteriostatic and fungistatic actions at low concentrations but bactericidal and fungicidal actions at high concentrations. The compounds 2a-c (Figure 6, Figure 7, Figure 8) showed greater antibacterial and anti-fungal activities than ethacridine (Petrikaite et al, 2007).

**Antitumor Activity of Acridine Derivatives**

A new class of Thiazacridine analogues were synthesised by a combination of acridine and thiazolidine nucleus and investigated their cytotoxic activity against human colon carcinoma HCT-8 cells. In which four compounds synthesised named as Ac-4, Ac-7, Ac-10, Ac-23(Figure 9). The synthesised compounds were proved to reduce the proliferation of
HCT-8 cells in a concentration and time-dependent manner. A marked increase in intra nucleosomal DNA fragmentation was achieved without altering the membrane integrity. Hematoxylin-eosin and acridine orange/ethidium bromide dyes were used to stain HCT-8 cells treated with synthesised compounds to observe the morphological changes under a light microscope. Cells were pelleted and resuspended with 25 µl of PBS then mixed with 1 µl of acridine orange/ethidium bromide solution and the morphological changes were observed under a fluorescence microscope.

The integrity of the cell membrane was assessed by using the exclusion of propidium ioddide and flow cytometric principles were used to determine the cell fluorescence. Cell cycle distribution was determined by harvested the cells in a solution of citrate 0.1%, Triton X-100 0.1% and propidium ioddide 50 µg/ml and the cell fluorescence was determined by flow cytometry. The mitochondrial transmembrane potential was measured by rhodamine 123 dye method. In which the cells were washed with PBS and incubated with rhodamine 123 at 37°C and the cell fluorescence was measured by flow cytometry. Phosphatidyl serine externalisation was determined by washed the cells with cold PBS and resuspended in 135 µl of PBS and with 5 µl of 7-amino actinomycin D (7AAd) and 10 µl of annexin V-PE and incubated at room temperature for 20 minutes and the cell activity measured by flow cytometry. Caspase 3/7 activity was analysed by the cells incubated with fluorescently labelled inhibitor and suspended with wash buffer after the incubation of prescribed time duration then centrifuged. The pellet was resuspended in the solution of propidium ioddide and wash buffer then immediately analysed by flow cytometry. Drop test assay was performed to determine the sensitivity of mutant S.Cerevisiae with defective topoisomerases. DNA relaxation assay was performed Topo I drug screening kit. The isolated lymphocytes determined genotoxicity in human lymphocytes were mixed with RPMI 1640 supplemented with 20% foetal bovine serum, phytohemagglutinin, two mM glutamine, 100U/ml penicillin and 100 µg/ml of streptomycin at 37°C with 5% CO₂. Finally, the cell viability was determined by trypan blue assay method—alkaline (PH <13) comet assay was performed by using single-cell gel electrophoresis. The damage index (DI) was calculated by migration length and amount of DNA in the tail. Chromosome aberration assay was performed. Doxorubicin was used as the positive control. Synthesised compounds added at prescribed concentrations to the culture after the incubation cells were harvested and treated with 0.075M KCl at 37°C for 20 minutes then stained with 3% Giemsa solution and focused under a light microscope to determine the frequency of CAS and the mitotic index. Telomerase inhibition assay was performed by determining the length of telomere using fluorescence in situ hybridisation with probes to telomeric sequences. The images were processed using the TFL-TELO software (Barros et al., 2013).

The anti-telomerase activity of BRACO-19(3,6,9-trisubstituted acridine 9-[4-(N,N-dimethlamino)phenylamino]-3,6-bis(3-pyrrrolidinopropionamido) acridine) was directed for the researchers to evaluate the anti-tumour activity. Since the telomerase complex is responsible for telomere maintenance, so it was believed that anti telomerase agents could exhibit potent anti-cancer activity. In this investigation a small molecule with anti telomerase activity designed by molecular modelling in a supercomputer to achieve significant interaction with G-Quadruplex region of DNA to form telomeric DNA to produce complete inhibition of the activity of telomerase.

One another surprising fact found in these studies is BRACO-19 did not produce non-specific acute cytotoxicity at same concentrations to those needed to inhibit an entire activity of telomerase. When BRACO-19 tested against 21NT human breast cancer cells results in a significant reduction of cell growth after only 15 days. The reduction of intracellular telomerase activity was indicated by a marked increase in the number of β-Galactosidase positive staining cells. In vivo anti-cancer activity is evaluated by intraperitoneal administration of 2mg/kg body weight of BRACO-19 to the mice having advanced stage A431 human vulval carcinoma previously treated with paclitaxel-induced antitumour effect and compared the observations with the group treated with paclitaxel alone. From these studies, it was concluded that BRACO-19 first choice of the second generation of G-Quadruplex mediated telomerase/telomere interactive compounds (Sharon et al., 2002).

Since telomeric integrity is an essential factor for replication of cancer cells, so it is considered as a target for the G-quadruplex–stabilising drug 3,11-difluoro-6,8,13-trimethyl-8H-quino[4,3,2-k]acridinium methosulfate in this study. It was proved a senescent-like growth arrest in MCF-7 breast cancer cells, within 14 to 17 days, and a reduction in telomere length (from 5.2 kilobases (kb) to 4.7 and 4.3 kb after 17 days of treatment at 0.5 and 1 µM, respectively). This compound does not exhibit cytotoxicity at therapeutic concentrations (doses < 1 µM over a 14-day exposure),
and it was found to be compatible even with long-term treatment. MCF-7 cells were ten times more sensitive to synthesised compounds compared with wild-type (wt) hTERT-expressing, vector-transfected control cells (longer TRF-length 5.2 kb; IC$_{50}$ 2 μM) in the 5 day SRB assay. This relationship was validated in a section of 36 human tumour xenografts grown in vitro positively correlated between telomere length and growth-inhibitory potency of RHPS4 (15-day clonogenic assay, r = 0.75). Those observations are constant with loss of the protective capping status of telomeres mediated by RHPS4 G-quadruplex-stabilization, thus leading to the greater susceptibility of cells with shorter telomeres. Combination studies were carried out with paclitaxel (Taxol), doxorubicin (Adriamycin), and the experimental therapeutic agent 17-(allylamino)-17-dimethoxy geldanamycin, which inhibits the 90-kDa heat shock protein, conferred enhanced sensitivity in RHPS4 treated MCF-7 cells. In contrast, the DNA-interactive temozolomide and cisplatin antagonised the action of RHPS4. Experimental results suggested the combination of certain classes of existing anti-cancer agents with this synthesised compound would be synergistic (Cookson et al., 2005).

**Anti Inflammatory Activity of Acridine Derivatives**

Anti-inflammatory, analgesic and kinase inhibition activities are evaluated with novel acridine derivatives. Those analogues are synthesised by condensation of 9-chloro-2,4-(un) substituted acridines with sulphanilamide derivatives such as sulphadiazine, sulphathiazole and sulfacetamide (3a-3h) and 3-Aryl -4-phenyl -2-imino-4-thiazolines (5a-5h). The condensation products were purified by chromatography or crystallisation. Anti-inflammatory activity was evaluated by using carrageenan-induced paw oedema in which albino rat model was used.0.1 ml of 1% solution Carrageenan was used as an irritant to develop oedema by administered into planter aponeurosis. The volume of the oedema was measured before and after the administration of solutions of standard drug and our synthesised analogues. The analgesic activity was measured by the writhing assay method in which the aqueous solution of phenyl quinone was administered intraperitoneally to the animal groups. The number of writhes recorded for 20 minutes, and the same was repeated after the administration of our test solutions containing desired concentrations of synthesised substances and standard. Compounds 5a,5c,5g (Figure 10 & Table 2) showed excellent anti-inflammatory activity, and compounds 3e (Figure 11), 5m (Figure 12) showed a significant analgesic activity (Sham et al., 2004).

Acridine derivatives (9-Anlino &9-Phenoxy) were synthesised and subjected to the evaluation of anti-inflammatory activity studies on the inhibitory effect of the suppression of activation of a mast cell, neutrophils and macrophages. Synthesised compounds showed a potent anti-inflammatory activity than reference standard and also exhibited a potent inhibitory effect on the secretion of lysosomal enzyme and β-glucuronidase from neutrophil. Some compounds also inhibit TNF α production macrophage-like cell line Raw 264.7. The synthesised compounds were found to be a potent inhibitor of TNF α production in microglial cell lines 94, and it was also observed that there was no significant cytotoxicity in those acridine derivatives (Chen et al., 2002).

**Anti Leishmanial Activity of Acridine Derivatives**

A quantitative structure-activity relationship has carried out with acridine derivatives for anti leishmanial activity. In this study molecular structures of totally 60 molecules of differently substituted acridines involved. Multiple linear regression and artificial neural network methods used to study, interpret and predict the activity of the newly designed molecules. The used descriptors are figured with gaussian 03, ACD/Chemsketch, Marvin sketch and chem office programs. The QSAR models established were validated based on principles framed by OECD. The descriptors are highly correlated with the activity were selected by principal component analysis (PCA). The dataset was divided into training sets and test sets by univariate partitioning (UP) method. The correlation coefficient calculated by multiple linear regression (MLR) equations. The correlation coefficient values were found to be 0.850, and 0.814 for anti leishmanial activities against promastigotes and amastigotes forms parasites respectively and validated by both internal and external validation methods and the statistical quality of QSAR models determined. The correlation coefficient of the descriptors acquired from the MLR in the artificial neural network was found to be 0.933 and 0.918 with 7-3-1 and 6-3-1 for antileishmanial activities against promastigotes and amastigotes forms of parasites, respectively (Chitta et al., 2016).

A series of 9-anilino acridines were synthesised and screened for the anti leishmanial activity against both the promastigote and amastigote forms of a parasite. It was assumed that anti leishmanial activity is due to the Topoisomerase-II inhibitory activity of substituted 9-anilino acridines. In this study 1, NH-hexyl compound prepared and confirmed it’s
activity and toxicity to mammalian cells also determined by using human leukaemia cell line. Then it was considered as Lead. Substitution pattern of 3,6-di(di methyl amino) group dramatically increases the antileishmanial activity without increasing the toxicity towards mammalian cells. The substitution of 2-OMe and 6-Cl also brought potent antileishmanial activity. Substitution of N(R)₂ at the acridine molecule leads to beneficial antileishmanial compound. This study was revealed that highly electron-donating lipophilic substitutions at the position -1 of 9-Anilino acridines make a potent antileishmanial compound (Gamage et al., 1997).

CONCLUSION

Bacterial, parasitic and viral infections are still a challenging task for physicians, of course, the acridine usage is limited due to some side effects and tumour resistance even though so many potent drug candidates can be derived from acridine nucleus with expected safety profile. It can be achieved by molecular modification; for example, acronycine the moderately potent and low water-soluble compound can be improved by molecular modification leads to the effective and highly water-soluble compound. Some of the acridine derivatives shown multiple pharmacological activities, for example, quinacrine was invented for the treatment of malaria but also exhibited remarkable anti-cancer activity which will give the useful information of the pharmacophore for the various targets. The strong cationic region of acridine dyes was found to be essential for their anti-microbial activity. The most important limiting factor governing the anti-microbial activity of acridines is the degree of ionisation. Tacrine is an anti-Alzheimer drug, but it’s usage become limited so the structure may be modified to produce new agent with improved efficacy and less toxicity. The drug repurposing studies also provide some useful information to produce novel therapeutic agents. This study reveals that the acridine/acridone moiety can provide so many lead molecules which can be modified further to obtain new, safe and effective drug candidate for bacterial, viral, fungal, parasitic and malarial infections. Our overall aim is to motivate the researchers to focus on the above mentioned key points to generate a safe and potent molecule from acridine to manage the challenging tasks of various diseases.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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