Before discussing the results of the present experiments, it is pertinent to provide updated information about the relevant literature reports. Hence, in consistent with the proposed work (as mentioned in the introductory part), the available literature information about the (A) development of ATP/ADP selective probes, (B) retro-aldolase model and (C) anti-cancer agents is given.

A. **Acridine based molecular probes.**

A number of acridine based cation selective, anion selective, pH sensitive, ATP selective and DNA binding probes are developed for the detection of ions, biological materials and monitoring of the biochemical pathways.

**Acridine based cation selective probes:**

![Chart 1](chart1.png)

As a simplest case, probe $1^1$ (Chart 1) undergoes quenching of fluorescence in presence of $\text{Cr}^{3+}$. Probe $2^2$ (Chart 1) also shows enhancement of fluorescence in the presence of $\text{Cr}^{3+}$ and the complex $2-\text{Cr}^{3+}$ undergoes quenching on addition of $\text{PO}_4^{3-}$. Further, probe $3^3$ (Chart 1) exhibits quenching of fluorescence with $\text{Cu}^{2+}$ in SDS micelle
at pH 2 and pH 8. In the presence of TX micelle, 3 shows enhancement with Cu$^{2+}$ at pH8. Acridine based probe 4 (Chart 1) exhibits enhancement in fluorescence in the presence of Zn$^{2+}$ at neutral pH whereas compound 5 (Chart 1) shows similar effect in the presence of Cd$^{2+}$. Probe 6 (Chart 1) is selective to Hg$^{2+}$ and fluorescence enhancement is reported at pH 6.0.

**Acridine based anion selective probes:**

Chemosensor 7 (Chart 2) exhibits quenching of fluorescence with the incremental addition of CN$^-$ (DMSO-water, 95:5 v/v as the medium) whereas probe 8 (Chart 2) shows enhancement in the fluorescence intensity in the presence of HCO$_3^-$.

Some of the acridine based fluorescent indicator dyes 9-16 (Chart 2) undergo fluorescence quenching on addition of Cl$^-$ in the aqueous medium. Acridine based receptors 17 (Chart 2) was showing selective interaction with H$_2$PO$_4^-$ which results in fluorescence enhancement.

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**Chart 2**
Acridine based pH sensitive probes:

Protonation – deprotonation of compound 18\textsuperscript{11} (Chart 3) at different pH of the solution make it to undergo change in fluorescence intensity and $\lambda_{em}$. Acridine based fluorescent probe 19\textsuperscript{12} (Chart 3) shows quenching of fluorescence with the change in pH from 4.2 to 10.0 in the phosphate buffer. Probe 19 also shows change in fluorescence in the presence of DNA in phosphate buffer. The acridine based fluorescent sensor 20\textsuperscript{13} (Chart 3) undergoes quenching of fluorescence when pH of the solution was changed from 3 to 12. The fluorescent probe 21\textsuperscript{14} also exhibits fluorescence quenching with the change in pH from 0.77 to 14.0.

\begin{center}
\includegraphics[width=\textwidth]{chart3.png}
\end{center}

Chart 3

Acridine based ATP selective probes:

The fluorescent probes 22-24\textsuperscript{15} (Chart 4) are selectively showing the quenching in fluorescence with addition of ATP in HEPES buffer. Probe 22 was also employed for the monitoring of the biochemical reactions.

\begin{center}
\includegraphics[width=\textwidth]{chart4.png}
\end{center}

Chart 4
Acridine based DNA binding probes:

The planar geometry of the acridine molecule makes it suitable to intercalate with DNA. Interactions of compounds 25-30\textsuperscript{16-18} (Chart 5) with DNA are studied by monitoring the change in fluorescence and UV-vis absorption of the compound – DNA solutions.

![Chart 5](image)

Other acridine based fluorescent probes:

In addition to the above reports, acridine based fluorescent probe 31\textsuperscript{19} (Chart 6) shows interaction with acetylcholinesterase. Probe 32\textsuperscript{20} (Chart 6) is used as fluorophore for tracking the protein-protein interactions and stability of the protein whereas probe 33\textsuperscript{21} (Chart 6) shows interaction with bovine albumin serum protein. It is also used as photosensitizer in photodynamic therapy. The biosensor 34\textsuperscript{22} (Chart 6) is used as electrochemical indicator to detect the nuclear factor kappa B in serum.

![Chart 6](image)
(B) Retro-aldolase model

Inspired by the catalytic features of aldolase during the glycolysis pathway, a number of enzyme models are developed for catalyzing the aldol and reteroaldol condensation reactions. Crystal structure of aldolase enzyme in complex with fructose bisphosphate (Figure 1) shows the presence of Lys, Tyr, Asp, Arg and His residues in the active site. During the catalytic phase of the enzyme (Figure 2), Lys and Tyr play a key role for the breakdown of fructose bisphosphate into glyceraldehyde and dihydroxyacetone phosphate.

![Figure 1. Active sites of aldolase enzyme.](image)

![Figure 2. Mechanism of aldolase enzyme with fructose bisphosphate as the substrate.](image)
Organocatalysts for aldol condensation reaction:

A number of reactions are reported in which the amino acids catalyze aldol condensation reaction. Condensation of $p$-nitrobenzaldehyde and cyclohexanone in water at room temperature (Scheme 1) is catalyzed by Ala (35) to yield the product (32%) whereas the product yield is increased in the presence of other amino acids or their derivatives24,25 (Table 1, Chart 7).

\[
\text{Scheme 1}
\]

Table 1. Use of catalyst in the reaction of scheme 1 and % yield thereof (refer to chart 7 for catalyst).

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Catalyst</th>
<th>% Yield</th>
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<tr>
<td>1</td>
<td>36</td>
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<tr>
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<td>88</td>
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</tbody>
</table>
Organocatalysts for reteroadol condensation reaction:

Besides the organocatalyzed aldol condensation reactions, peptide based catalysts are reported for retero aldol condensation reaction. β-Peptides 53-55 (Chart 8) catalyze the retroaldol cleavage of 4-phenyl-4-hydroxy-2-oxobutyrate into benzaldehyde and pyruvate (Scheme 3) though their catalytic properties are different.

Scheme 3
Peptides\textsuperscript{27} FT-YLK-3, YLK-18-opt and aldolase antibody 38C2\textsuperscript{28} catalyze the reteroaldol reaction (Scheme 4) with C-C bond cleavage.

\begin{equation}
\text{FT-YLK-3} \xrightarrow{\text{YLK-18-opt}} \text{dehyde} + \text{hydroxy benzene}
\end{equation}

\textbf{Scheme 4}

(C) \textbf{Acridine based Anti-cancer agents}

A number of acridine derivatives, targeting the cellular factors like DNA, topoisomerase, telomere and cell cycle etc are developed for cancer therapy.
Acridine based DNA intercalators as anticancer agents:

Compounds 56-59\(^3\) (Chart 9) show good antiproliferative activity on L1210 and KB-3-1 cell lines whereas compound 58 causes alkylation of DNA guanine units. Compound 60\(^3\) (Chart 9) with significant DNA binding property was active for the antitumor activity.
Compounds 61-64\textsuperscript{34} (Chart 9) are reported to have DNA binding features and show anticancer activity against 60 human tumor cell lines. The anticancer activity of compounds 65-70\textsuperscript{35-37} (Chart 10) is mainly due to their intercalation with DNA.

**Chart 10**

**Acridine based topoisomerase inhibitors as anticancer agents:**

Their significant role during the process of DNA replication makes DNA topoisomerase as the potential cellular target of anticancer drugs. Acridine derivative 71\textsuperscript{38} (Chart 11) shows cytotoxicity against human cancerous cells and it is found to inhibit the catalytic activity of topoisomerases. Compound 72\textsuperscript{39} and 73\textsuperscript{40} (Chart 11) also exhibit similar mode of action for their anticancer activity.
Acridine based telomere inhibitors as anticancer agents:

Telomere protects the chromosomes from degradation and plays important role in the cell division and cell viability. These features of telomere make it the target of many reported anticancer drugs. Compound 74-75\textsuperscript{41} (Chart 12) exhibit antiproliferative activity due to the telomere inhibition.

Cell cycle arrest by acridine based anticancer agents:

Arrest of cell division at the G0/G1, G2 and M phases is another strategic approach to tackle propagation of cancer. Hence, along with topoisomerase and telomeres, cell cycle is the important target of anticancer drugs. Compound 76-77\textsuperscript{42} (Chart 13) were active for the antiproliferative activity against human cancer cell lines by cell cycle arrest. Similarly, compound 78-79\textsuperscript{43} (Chart 13) also exhibit antitumor activity with cell cycle inhibition.
Therefore it is apparent from the brief review of literature that the acridine template is a versatile synthon. Besides acting as the fluorescent moiety, its biological acceptance and planar geometry also provide unique features to the molecule. The acridine based molecules are found to interact with DNA, ATP, ADP and some specific enzymes.

REFERENCES


