Functionalized Non-Steroidal Anti-Inflammatory Drugs (NSAID) for Controlled Release Applications
FUNCTIONALIZED DRUG MOLECULES

At Bezwada Biomedical, motivations to control the rate of release of drug molecules from a few hours to months formed the basis of the development of novel absorbable linear and multi-armed oligomers of glycolide, lactide, p-dioxanone and caprolactone wherein the end groups have been functionalized with therapeutically active drug molecules. These molecules are the key components of commercially available absorbable medical devices. Functionalized drugs oligomers are expected to release drug in a controlled manner at the site of action which will increase the efficacy of this drug over a long period of time. It will also help to increase the solubility of the drug. In contrast to literature reported polyanhydrides and polyester-anhydride polymers incorporating anti-inflammatory drug molecules such as Aspirin in the polymer backbone chain, the oligomers and polymers developed by our company have a much faster degradation profile and are much easier to handle and process. Moreover, the hydrolysis results in the release of the drug molecule as such, thus preserving the therapeutic activity of the drug molecule.

Bezwada Biomedical is pleased to provide a portfolio of functionalized Non-Steroidal Drug molecules which can be used either as such or as monomers for preparation of absorbable therapeutic polymers which incorporate drug molecules in the polymer backbone chain for extended and controlled release applications.

Nonsteroidal anti-inflammatory drugs are the ones that exhibit anti-inflammatory, analgesic and antipyretic (fever-reducing) effects. The most prominent NSAIDs sold under various trade names are Advil, Motrin, Nuprin Aleve, Naprosyn and Celebrex. They are usually indicated for the treatment of mild to moderate pain and associated swelling and inflammation. Research continues into their potential to prevent the occurrence of colorectal cancer and other conditions such as cardiovascular problems.
NSAIDs work primarily by inhibiting the action of the enzyme cyclooxygenase which plays a key role in the blocking the production of hormones called prostaglandins. Most NSAIDs block two different enzymes, called Cox-1 and Cox-2 that the body uses to make prostaglandins. Prostaglandins help cause pain, inflammation, fever, muscle cramps and aches. Hence, by inhibiting the action of enzyme cyclooxygenase, NSAIDs block prostaglandin formation thereby alleviating symptoms of pain and inflammation. All of the NSAIDs work in much the same way as Aspirin, which has been used for more than 2,000 years to treat pain. At low doses, the NSAIDs work essentially as pain relievers. At higher doses, they can reduce the body’s inflammatory response to tissue damage, as well as relieve pain.

![Figure 1 Common Anti-inflammatory Drug Molecules](image)

NSAIDs are generally used in the treatment for the symptomatic relief of the following conditions:

- Rheumatoid arthriitis
- Osteoarthritis
- Inflammatory arthropathies that include ankylosing spondylitis, psoriatic arthritis and Reiter's syndrome
- Acute gout
- Menstrual pain
- Metastatic bone pain
- Headache and migraine
- Postoperative pain
- Mild-to-moderate pain due to inflammation and tissue injury
- Pyrexia (fever)
- Ileus

**Table 1** List of common NSAID with their activities are listed below

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Activities</th>
</tr>
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<tbody>
<tr>
<td><img src="image" alt="Aspirin" /></td>
<td>Aspirin causes several effects on the body. As an analgesic, it to relieve minor aches and pains, as an antipyretic, it is used to reduce fever, as an anti-inflammatory, it reduces inflammation. In addition, it prevents clotting</td>
</tr>
<tr>
<td><img src="image" alt="Diclofenac" /></td>
<td>Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) used to reduce inflammatory disorders. It is also used as an analgesic for reducing pain in certain conditions.</td>
</tr>
<tr>
<td>Drug</td>
<td>Description</td>
</tr>
<tr>
<td>------</td>
<td>-------------</td>
</tr>
<tr>
<td>Naproxen</td>
<td>Naproxen is a nonsteroidal anti inflammatory drug. It has analgesic and antipyretic properties. It is used to relieve pain, tenderness, swelling, and stiffness caused by osteoarthritis, rheumatoid arthritis, juvenile arthritis and ankylosing spondylitis.</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>Ketoprofen is a nonsteroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic effects. Ketoprofen is generally prescribed for arthritis-related inflammatory pains or severe toothaches that result in the inflammation of the gums.</td>
</tr>
<tr>
<td>Fenbufen</td>
<td>Fenbufen is used to treat inflammation as in osteoarthritis, ankylosing spondylitis, and tendinitis. In addition, it can also be used to relieve backaches, sprains, and fractures.</td>
</tr>
<tr>
<td>Suprofen</td>
<td>Suprofen is a Non-steroidal anti-inflammatory drug (NSAID). It is anti-inflammatory, analgesic and antipyretic drug and has been shown to be effective in the relief of acute and chronic pain associated with arthritis.</td>
</tr>
<tr>
<td>Diflunisal</td>
<td>Diflunisal is a non-steroidal anti-inflammatory drug (NSAID). It also has an antipyretic effect. Diflunisal is used to relieve pain, tenderness, swelling and stiffness caused by osteoarthritis (arthritis caused by a breakdown of the lining of the joints) and rheumatoid arthritis.</td>
</tr>
<tr>
<td><strong>Diflunisal</strong></td>
<td>Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID). It has analgesic and anti-pyretic properties. It is used for relief of symptoms of arthritis, fever and pain.</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td><strong>Ibuprofen</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Lumiracoxib</strong></td>
<td>Lumiracoxib is a COX-2 selective inhibitor drug.</td>
</tr>
<tr>
<td><strong>Tolmetin</strong></td>
<td>Tolmetin is a non-steroidal anti-inflammatory drug of the arylalkanoic acids. It is used primarily to reduce hormones that cause pain, swelling, tenderness, and stiffness in conditions such as osteoarthritis and rheumatoid arthritis, including juvenile rheumatoid arthritis.</td>
</tr>
<tr>
<td><strong>Mefenamic Acid</strong></td>
<td>Mefenamic is used in treatment of pain, including menstrual cramps. Mefenamic acid decreases inflammation and uterine contractions by a still unknown mechanism. There is also evidence that supports the use of mefenamic acid for perimenstrual migraine headache prophylaxis</td>
</tr>
<tr>
<td><strong>Loxoprofen</strong></td>
<td>Loxoprofen belongs to propionic acid derivatives group. It belongs to the same chemical family as ibuprofen, naproxen and ketoprofen. It is used in treatment of musculoskeletal and joint disorders. Loxoprofen is a prodrug and is administered in inactive form. Once administered, the prodrug is metabolized in vivo into an active metabolite.</td>
</tr>
</tbody>
</table>
Tiaprofenic Acid

Tiaprofenic belongs to arylpropionic acid (profen) class. It is used to treat pain, especially arthritic pain, with indications for osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, periarticular disorders, and strains and sprains.

Ketorolac

Ketorolac is a non-steroidal anti-inflammatory drug (NSAID) in the family of heterocyclic acetic acid derivatives, often used as an analgesic. Ketorolac acts by inhibiting the bodily synthesis of prostaglandins.

**Controlled Release Of Nonsteroidal Anti-Inflammatory Drugs**

At Bezwada Biomedical, motivations to control the rate of release of NSAID drug molecules from a few hours to months formed the basis of the development of novel absorbable linear and multi-armed oligomers of glycolide, lactide, p-dioxanone and caprolactone wherein the end groups have been functionalized with therapeutically active non-steroidal drug molecules. These molecules are the key components of commercially available absorbable medical devices. Functionalized NSAID drug molecules and oligomers are expected to release drug in a controlled manner at the site of action which will increase the efficacy of this drug over a long period of time. It will also help to increase the solubility of the drug. In contrast to literature reported polyanhydrides and polyester-anhydride polymers incorporating anti-inflammatory drug molecules such as Aspirin in the polymer backbone chain, the oligomers and polymers developed by our company have a much faster degradation profile and are much easier to handle and process. Moreover, the hydrolysis results in the release of the drug molecule as such, thus preserving the therapeutic activity of the drug molecule.
In summary, the functionalized non-steroidal anti-inflammatory drug molecules, oligomers and absorbable polymers incorporating these functionalized drug molecules developed and offered by our company provides the following advantages against the competing technologies:

- Drug molecule is a part of the absorbable therapeutic polymer backbone. The polymer upon hydrolysis in-situ releases the drug molecule as such at the site. This prevents or minimizes premature loss of efficacy of the drug while eliminating the associated side effects.
- The drug molecule forms a significant component of the polymer backbone resulting in a delivery of a highly effective and potent dose.
- The rate of release of drug molecule can be controlled at the site of action by the structure of the polymer leading to no-burst effects in delivery.
- There is no need to use excipients or solubility modifiers, as the drug is incorporated into polymer architecture. This eliminates issues associated with compatibility.
- The polymers comprised of these functionalized drug molecules are highly likely to be radiation, gamma and EtO sterilizable.
**Potential Applications**

These functionalized non-steroidal drug molecules, absorbable oligomers and polymers with a controlled degradation profile, have potential applications in the same or similar areas as the non-functionalized drug molecule. This is attributed to the release of the drug molecule as such over a period of time upon hydrolysis of the end-functionalized oligomers and polymers. Some of the key application areas for these functionaled drug molecules include controlled drug delivery, formulations for pain management, wound healing, topical therapeutic creams and cosmetic applications. Specific focus areas include:

- Arthritis
- Sports injuries
- Advanced wound repair
- Veterinary applications
- Topical analgesic and anti-inflammatory creams

**Contact Us**

*For further information on how we can help you engineer your success, please contact us at rao@bezwadabiomedical.com, or visit us at www.bezwadabiomedical.com*

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To place an order, please write or fax to:

Bezwada Biomedical LLC
15 Ilene Court, Suite 1
Hillsborough, NJ 08844 U.S.A.
Telephone: (908) 281-7529 Fax: (908) 359-1179
e-mail: info@bezwadabiomedical.com

Specify the chemical name, the catalog number, the quantity and your purchase order number.

Terms and conditions of sale:
Terms are F.O.B. Hillsborough, New Jersey. Net 10 days. Prices shown are in U.S. dollars and are subject to change. All orders are insured at the buyers’ expense. Applicable taxes and shipping charges will be added to the invoice.
Chemicals marked “with HPLC” or “with GC” are supplied with an actual analysis as determined by high-pressure liquid chromatography or gas chromatography, respectively. These compounds have catalog numbers with suffix letter S.

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Please inquire for substantial savings on bulk quantities or standing annual requirements.

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Delivery:
Period of delivery will be given upon receipt of an inquiry or order.
Aspirin causes several effects on the body. As an analgesic, it is used to relieve minor aches and pains, as an antipyretic, it is used to reduce fever, as an anti-inflammatory, it is used to reduce inflammation. In addition, it prevents clotting. Salicylic acid, the main metabolite of aspirin, is an integral part of human and animal metabolism.

Aspirin also shows antiplatelet effect by inhibiting the production of thromboxane. Thromboxane under normal circumstances binds the platelet molecules together to create a patch over damaged walls of blood vessels. When this patch starts growing, it can block the blood flow resulting in acute occlusive vascular events. The decreased platelet aggregation caused by Aspirin helps to prevent heart attacks, strokes, and blood clot formation in people at high risk of developing blood clots. Low-dose, long-term use of Aspirin irreversibly blocks the formation of thromboxane \( A_2 \) in platelets, producing an inhibitory effect on aggregation. Many people take a daily aspirin to reduce their risk of heart attack. Recent studies have suggested that Aspirin reduces the long-term risk of death due to cancer. Their finding suggested that Aspirin might help in treatment of some cancers and provides proof of principle for pharmacological intervention specifically to prevent distant metastasis.

**Functionalized Aspirin**

Wide spectrum therapeutic potential of this compound motivated us to enhance its bioavailability over extended period of time by functionalizing it with safe and biocompatible molecules such as glycolic acid, lactic acid, caprolactone and \( p \)-dioxanone. These molecules are the key components of commercially available absorbable medical devices. Functionalized Aspirin oligomers are expected to release Aspirin in a controlled manner at the site of action which will
increase the efficacy of this drug over a long period of time. It will also help to increase the solubility of the drug. Finally, these hydrolysable Aspirin compounds are expected to have improved bioavailability, improved efficacy and are also anticipated to degrade into safe and biocompatible molecules.

References

4. Bezwada, Rao S. Controlled release of biologically active compounds from multi-armed oligomers. US Patent No. 8, 163, 806.

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MW 408.44

C_{26}H_{28}O_6
MW 502.42
mp 91-92.5°C
White powder
Soluble in chloroform
Structure confirmed by NMR

C_{26}H_{26}O_6
MW 530.48

C_{26}H_{30}O_4
MW 590.53

19-2570 6-[6-(2-Acetoxybenzoyl)oxyhexanoyloxy]ethoxy]-6-oxo-hexyl] 2-acetoxybenzoate
C_{32}H_{38}O_12
MW 614.64
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| 19-1114 | [2-[2-[2-(Acetoxybenzoyl)oxyacetyl]oxyethoxy]-2-oxo-ethyl] 2-acetoxybenzoate; (2-oxo-2-propoxy-ethyl) 2-acetoxybenzoate  
**Aspirin Trimer**  
C_{38}H_{38}O_{18}  
MW 782.70  
Light yellow syrup  
Soluble in chloroform  
Structure confirmed by NMR |
**Aspirin Trimer**  
C_{41}H_{44}O_{18}  
MW 824.78 |
**Aspirin Trimer**  
C_{44}H_{50}O_{21}  
MW 914.86 |
| 19-2573 | [6-[2-[6-(Acetoxybenzoyl)oxyhexanoyloxy]ethoxy]-6-oxo-hexyl] 2-acetoxybenzoate; (6-oxo-6-propoxy-hexyl) 2-acetoxybenzoate  
**Aspirin Trimer**  
C_{50}H_{62}O_{18}  
MW 951.02 |
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<td>C_{49}H_{48}O_{24}</td>
<td>MW 1020.89, mp 90.5-93.5°C, White powder, Soluble in DMF, Structure confirmed by NMR</td>
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<td>C_{53}H_{56}O_{24}</td>
<td>MW 1077</td>
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<td>2-[2-[2-(2-Acetoxybenzoyl)oxyethoxy]acetyl]oxyethoxy]-2-oxo-ethoxy]ethyl 2-acetoxybenzoate (Aspirin Tetramer)</td>
<td>C_{56}H_{60}O_{28}</td>
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<td>19-2576</td>
<td>[6-[2-(6-(2-Acetoxybenzoyl)oxyhexanoyloxyethoxy]-6-oxo-hexyl] 2-acetoxybenzoate (Aspirin Tetramer)</td>
<td>C_{64}H_{76}O_{24}</td>
<td>MW 1229.27</td>
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</table>
Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) used to reduce inflammatory disorders. It is also used as an analgesic for reducing pain in certain conditions. As an anti-inflammatory it is used in treatment of arthritis, rheumatoid arthritis, polymyositis, dermatomyositis, osteoarthritis, dental pain, TMJ, spondylarthritis, ankylosing spondylitis, gout attacks. As an analgesic it is used in pain management in cases of kidney stones and gallstones. Diclofenac is often used to treat chronic pain associated with cancer, in particular if inflammation is also present. Good results have been seen in female breast cancer and in the pain associated with bony metastases. It is marketed under the trade names Anuva, Abitren, Befol, Berifen, Betaren, Cambia, Cataflam, Catafast, Dedolor, Deflamat, Feloran, Fenac, Klodifen, Motifene, Naklofen, Pritaren, Rapidus, Rufenal, Safeguard (combination with misoprostol), etc.

The mechanism responsible for its anti-inflammatory, antipyretic, and analgesic action is inhibition of prostaglandin synthesis by inhibition of cyclooxygenase (COX). It also appears to exhibit bacteriostatic activity by inhibiting bacterial DNA synthesis.

**Functionalized Diclofenac**

Wide spectrum therapeutic potential of this compound motivated us to enhance its bioavailability over extended period of time by functionalizing it with safe and biocompatible molecules such as glycolic acid, lactic acid, caprolactone and p-dioxanone. These molecules are the key components of commercially available absorbable medical devices. Functionalized Diclofenac oligomers are expected to release Diclofenac in a controlled manner at the site of action which will increase the efficacy of this drug over a long period of time. It will also help to increase the
solubility of the drug. Finally, these hydrolysable Diclofenac compounds are expected to have improved bioavailability, improved efficacy and are also anticipated to degrade into safe and biocompatible molecules.

References:

2. Bezwada, Rao S. Controlled release of biologically active compounds from multi-armed oligomers. US Patent No. 8, 163, 806.

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   MW 500.32

19-2322 6-[6-[2-[2-(2,6-Dichloroanilino)phenyl]acetyl]oxyhexanoyloxy]hexanoic acid
   C_{26}H_{31}Cl_2NO_6
   MW 524.4

   C_{34}H_{28}Cl_4N_2O_8
   MW 734.41

   C_{36}H_{32}Cl_4N_2O_8
   MW 762.46

   C_{38}H_{36}Cl_4N_2O_{10}
   MW 822.51
19-2326  2-[6-[[2-(2,6-Dichloroanilino)phenyl]acetyl]oxyhexanoyloxy]ethyl 6-[2-(2,6-dichloroanilino)phenyl]acetyl]oxyhexanoate
\[C_{42}H_{44}Cl_4N_2O_8\]  MW 846.62

\[(\text{Diclofenac Trimer})\]  \[C_{53}H_{47}Cl_6N_3O_{12}\]  MW 1130.67

\[(\text{Diclofenac Trimer})\]  \[C_{56}H_{53}Cl_6N_3O_{12}\]  MW 1172.75

\[(\text{Diclofenac Trimer})\]  \[C_{59}H_{59}Cl_6N_3O_{15}\]  MW 1262.83
19-2330  
(Diclofenac Trimer)  
C_{65}H_{71}Cl_{16}N_{3}O_{12}  
MW 1298.99

19-2331  
(Diclofenac Tetramer)  
C_{68}H_{56}Cl_{8}N_{4}O_{16}  
MW 1468.81

19-2332  
(Diclofenac Tetramer)  
C_{72}H_{64}Cl_{8}N_{4}O_{16}  
MW 1524.92

19-2333  
(Diclofenac Tetramer)  
C_{76}H_{72}Cl_{8}N_{4}O_{20}  
MW 1645.02
C₈₄H₈₈Cl₈N₄O₁₆
MW 1693.24
Naproxen

Naproxen is a nonsteroidal anti-inflammatory drug. It has analgesic and antipyretic properties. It is used to relieve pain, tenderness, swelling, and stiffness caused by osteoarthritis, rheumatoid arthritis, juvenile arthritis and ankylosing spondylitis. Prescription naproxen tablets, extended-release tablets, and suspension are also used to relieve shoulder pain caused by bursitis, tendinitis, gouty arthritis, and pain from other causes. It is also used to reduce fever by changing the body’s thermostat in the brain. Naproxen is marketed under various trade names as Aleve, Anaprox, Antalgin, Nalgesin, Naposin, Naprelan, Narocin, Proxen, Synflex and Xenobid etc. Naproxen works by blocking the effect of certain hormones called prostaglandins which causes pain and inflammation in the body. Naproxen blocks the enzyme cyclooxygenase that makes prostaglandins, resulting in lower concentrations of prostaglandins. As a consequence, inflammation, pain and fever are reduced.

Functionalized Naproxen

Wide spectrum therapeutic potential of this compound motivated us to enhance its bioavailability over extended period of time by functionalizing it with safe and biocompatible molecules such as glycolic acid, lactic acid, caprolactone and p-dioxanone. These molecules are the key components of commercially available absorbable medical devices. Functionalized Naproxen oligomers are expected to release Naproxen in a controlled manner at the site of action which is expected to increase the efficacy of this drug over a long period of time. This functionalization also helps to increase the solubility of the drug. In addition, these hydrolysable Naproxen oligomers are expected to have improved bioavailability, improved efficacy and are also anticipated to degrade into safe and biocompatible molecules.
References:

2. Bezwada, Rao S. Controlled release of biologically active compounds from multi-armed oligomers. US Patent No.8,163,806.

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19-2335 2-[(2S)-2-(6-Methoxy-2-naphthyl)-propanoyl]oxyacetic acid
\[C_{16}H_{16}O_5\]
MW 288.30

19-2336 2-[(2S)-2-(6-Methoxy-2-naphthyl)propanoyl]oxypropanoic acid
\[C_{17}H_{18}O_6\]
MW 302.32

19-2337 2-[(2S)-2-(6-Methoxy-2-naphthyl)propanoyl]oxyethoxyacetic acid
\[C_{18}H_{20}O_6\]
MW 332.35

19-2338 6-[(2S)-2-(6-Methoxy-2-naphthyl)propanoyl]oxyhexanoic acid
\[C_{20}H_{22}O_5\]
MW 344.40

19-2339 2-[(2S)-2-(6-Methoxy-2-naphthyl)propanoyl]oxyacetyl]oxyacetic acid
\[C_{18}H_{18}O_7\]
MW 346.33

19-2340 2-[(2S)-2-(6-Methoxy-2-naphthyl)propanoyl]oxypropanoyloxy]propanoic acid
\[C_{20}H_{22}O_7\]
MW 374.38
C$_{25}$H$_{25}$O$_9$  
MW 434.44

19-2342 6-[6-[2-(6-Methoxy-2-naphthyl)propanoyl]oxyhexanoyloxy]hexanoic acid  
C$_{26}$H$_{34}$O$_7$  
MW 458.54

C$_{34}$H$_{34}$O$_{10}$  
MW 602.63

C$_{36}$H$_{38}$O$_{10}$  
MW 630.68

C$_{36}$H$_{42}$O$_{12}$  
MW 690.73

19-2346 2-[6-{2-(6-Methoxy-2-naphthyl)propanoyl]oxyhexanoyloxy}ethyl 6-{(2S)-2-(6-methoxy-2-naphthyl) propanoyl]oxyhexanoate  
C$_{38}$H$_{50}$O$_{12}$  
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MW 1205.28

(Naproxen Tetramer)
C_{72}H_{76}O_{20}
MW 1261.4

(Naproxen Tetramer)
C_{76}H_{84}O_{24}
MW 1380
(Naproxen Tetramer)
C₈₆H₁₀₀O₂₀
MW 1429.72
Ketoprofen is one of the propionic acid classes of nonsteroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic effects. Ketoprofen is generally prescribed for arthritis-related inflammatory pains or severe toothaches that result in the inflammation of the gums. Ketoprofen topical patches are being extensively used for treatment of musculoskeletal pain. The patches have been shown to provide rapid and sustained delivery to underlying tissues without significantly increasing levels of drug concentration in the blood when compared to the traditional oral administration. Ketoprofen is marketed under the brand name of Orudis and Oruvail in US. Its primary mode of action involves reducing the levels of prostaglandins, chemicals that are responsible for pain, fever, and inflammation. Ketoprofen reduces prostaglandins by blocking the enzyme cyclooxygenase. As a consequence, inflammation, pain and fever are reduced.

Wide spectrum therapeutic potential of this compound motivated us to enhance its bioavailability over extended period of time by functionalizing it with safe and biocompatible molecules such as glycolic acid, lactic acid, caprolactone and p-dioxanone. These molecules are the key components of commercially available absorbable medical devices. Functionalized Ketoprofen oligomers are expected to release Ketoprofen in a controlled manner at the site of action which will increase the efficacy of this drug over a long period of time. It will also help to increase the solubility of the drug. Finally, these hydrolysable Ketoprofen compounds are expected to have improved bioavailability, improved efficacy and are also anticipated to degrade into safe and biocompatible molecules.
References:

2. Bezwada, Rao S. Controlled release of biologically active compounds from multi-armed oligomers. US Patent No.8, 163, 806.

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Hillsborough, New Jersey 08844
32
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| 19-2371 | [2-2-2-[3-Benzoylphenyl]propanoyloxy|acetyl|oxyethoxy]-2-oxo-ethyl] 2-(3-benzoylphenyl)propanoate (Ketoprofen Tetramer)  
| C_{76}H_{68}O_{20}  
| MW 1301.38  |

| 19-2372 | [2-2-2-[3-Benzoylphenyl]propanoyloxy|propanoyloxy|ethoxy]-1-methyl-2-oxo-ethyl] 2-(3-benzoylphenyl)propanoate (Ketoprofen Tetramer)  
| C_{80}H_{76}O_{20}  
| MW 1357.48  |

| 19-2373 | 2-[2-[2-[2-(3-Benzoylphenyl)propanoyloxy|ethoxy|acetyl|oxyethoxy]-2-oxoethoxy|ethyl] 2-(3-benzoylphenyl)propanoate (Ketoprofen Tetramer)  
| C_{84}H_{84}O_{24}  
| MW 1477.6  |

| 19-2374 | 2-[6-[2-(3-Benzoylphenyl)propanoyloxy|hexanoyloxy|ethyl] 6-[2-(3-benzoylphenyl)acetyl|oxyhexanoate (Ketoprofen Tetramer)  
| C_{90}H_{96}O_{30}  
| MW 1497.76  |
Fenbufen is used to treat inflammation as in osteoarthritis, ankylosing spondylitis, and tendinitis. In addition, it can also be used to relieve backaches, sprains, and fractures. Fenbufen is sold with the brand names Cepal, Cinopal, Cybufen, Lederfen, and Reugast. Fenbufen works by blocking the action of enzyme cyclo-oxygenase (COX) involved in the production of various chemicals in the body, including prostaglandins. Prostaglandins are produced in response to injury and certain diseases and conditions, and cause pain, swelling and inflammation. By blocking the action of COX, it stops the production of these prostaglandins resulting in less pain and inflammation.

Wide spectrum therapeutic potential of this compound motivated us to enhance its bioavailability over extended period of time by functionalizing it with safe and biocompatible molecules such as glycolic acid, lactic acid, caprolactone and p-dioxanone dimers, trimers and tetramers. These molecules are the key components of commercially available absorbable medical devices. Functionalized Fenbufen oligomers are expected to release Fenbufen in a controlled manner at the site of action which will increase the efficacy of this drug over a long period of time. It will also help to increase the solubility of the drug. Finally, these hydrolysable Fenbufen compounds have improved bioavailability, improved efficacy and are also anticipated to degrade into safe and biocompatible molecules.
References:

2. Bezwada, Rao S. Controlled release of biologically active compounds from multi-armed oligomers. US Patent No. 8, 163, 806.

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19-2381  2-[2-[2-[4-Oxo-4-(4-phenylphenyl)butanoyl]oxyethoxy]acetyl]oxyethoxy]acetic acid  
   \( C_{24}H_{26}O_9 \)  
   MW 458.46  

19-2382  6-[6-[4-Oxo-4-(4-phenylphenyl)butanoyl]oxyhexanoyloxy]hexanoic acid  
   \( C_{28}H_{34}O_7 \)  
   MW 482.56  

   \( C_{30}H_{32}O_{10} \)  
   MW 650.69  

   \( C_{32}H_{34}O_{10} \)  
   MW 678.74  

   \( C_{32}H_{42}O_{12} \)  
   MW 738.80
19-2386 2-[6-[4-Oxo-4-(4-phenylphenyl)butanoyl]oxyhexanoyloxy]ethyl 6-[4-oxo-4-(4-phenylphenyl)butanoyl]oxyhexanoate
C_{46}H_{50}O_{10}
MW 762.91

(Fenbufen Trimer)
C_{56}H_{56}O_{15}
MW 1005.10

19-2388 [1-Methyl-2-oxo-2-[2-[2-[4-oxo-4-(4-phenylphenyl)butanoyl]oxypropanoyloxy]ethoxy]ethyl] 4-oxo-4-(4-phenylphenyl)butanoate; (1-methyl-2-oxo-2-propoxy-ethyl) 4-oxo-4-(4-phenylphenyl)butanoate
(Fenbufen Trimer)
C_{62}H_{62}O_{15}
MW 1047.17

19-2389 2-[2-Oxo-2-[2-[2-[4-oxo-4-(4-phenylphenyl)butanoyl]oxyethoxy]acetyl]oxyethoxy]ethoxy]ethyl 4-oxo-4-(4-phenylphenyl)butanoate; 2-(2-oxo-2-propoxy-ethoxy)ethyl 4-oxo-4-(4-phenylphenyl)butanoate
(Fenbufen Trimer)
C_{68}H_{68}O_{15}
MW 1173.42
19-2390  2-[6-[4-Oxo-4-(4-phenylphenyl)butanoyl]oxyhexanoyloxy]ethyl 6-[4-oxo-4-(4-phenylphenyl)butanoyl]oxyhexanoate; propyl 6-[4-oxo-4-(4-phenylphenyl)butanoyl]oxyhexanoate  
(Fenbufen Trimer)  
C_{71}H_{80}O_{15}  
MW 1173.38
Suprofen is a Non-steroidal anti-inflammatory drug (NSAID). It is anti-inflammatory, analgesic and antipyretic drug and has been shown to be effective in the relief of acute and chronic pain associated with arthritis. It is used as a topical ophthalmic solution, typically to prevent miosis during and after ophthalmic surgery.

Suprofen works by blocking the action of enzyme cyclo-oxygenase (COX) involved in the production of various chemicals in the body, including prostaglandins. Prostaglandins are produced in response to injury and certain diseases and conditions, and cause pain, swelling and inflammation. By blocking the action of COX, it stops the production of these prostaglandins resulting in less pain and inflammation.

Wide spectrum therapeutic potential of this compound motivated us to enhance its bioavailability over extended period of time by functionalizing it with safe and biocompatible molecules such as glycolic acid, lactic acid, caprolactone and p-dioxanone dimers, trimers and tetramers. These molecules are the key components of commercially available absorbable medical devices. Functionalized Suprofen oligomers are expected to release Suprofen in a controlled manner at the site of action which will increase the efficacy of this drug over a long period of time. It will also help to increase the solubility of the drug. Finally, these hydrolysable Suprofen compounds are expected to have improved bioavailability, improved efficacy and are also anticipated to degrade into safe and biocompatible molecules.
References:

2. Bezwada, Rao S. Controlled release of biologically active compounds from multi-armed oligomers. US Patent No.8, 163, 806.

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19-2391 2-[2-[3-(Thiophene-2-carbonyl)phenyl]acetyl]oxyacetic acid
   C₁₅H₁₂O₅S
   MW 304.32

19-2392 2-[2-[3-(Thiophene-2-carbonyl)phenyl]acetyl]oxypropanoic acid
   C₁₆H₁₄O₅S
   MW 318.34

19-2393 2-[2-[2-[3-(Thiophene-2-carbonyl)phenyl]acetyl]oxyethoxy]acetic acid
   C₁₇H₁₆O₆S
   MW 348.37

19-2394 6-[2-[3-(Thiophene-2-carbonyl)phenyl]acetyl]oxyhexanoic acid
   C₁₉H₂₀O₅S
   MW 360.42

19-2395 2-[2-[2-[3-(Thiophene-2-carbonyl)phenyl]acetyl]oxyacetyl]oxyacetic acid
   C₁₇H₁₄O₇S
   MW 362.35

   C₁₉H₁₈O₇S
   MW 390.41
\[\text{C}_{21}\text{H}_{22}\text{O}_{9}\text{S}\]  
MW 450.46

19-2398 6-[6-[3-(Thiophene-2-carbonyl)phenyl]acetyl]oxyhexanoyloxy]hexanoic acid  
\[\text{C}_{25}\text{H}_{30}\text{O}_{7}\text{S}\]  
MW 474.57

\[\text{C}_{32}\text{H}_{26}\text{O}_{10}\text{S}_{2}\]  
MW 634.69

\[\text{C}_{34}\text{H}_{30}\text{O}_{10}\text{S}_{2}\]  
MW 662.74

\[\text{C}_{36}\text{H}_{34}\text{O}_{12}\text{S}_{2}\]  
MW 722.79

\[\text{C}_{40}\text{H}_{42}\text{O}_{10}\text{S}_{2}\]  
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C\textsubscript{68}H\textsubscript{60}O\textsubscript{20}S\textsubscript{4}
MW 1325.48

C\textsubscript{64}H\textsubscript{52}O\textsubscript{20}S\textsubscript{4}
MW 1269.38

C\textsubscript{72}H\textsubscript{68}O\textsubscript{24}S\textsubscript{4}
MW 1445.58

C\textsubscript{90}H\textsubscript{84}O\textsubscript{30}S\textsubscript{4}
MW 1493.8
Diflunisal

Diflunisal is a non-steroidal anti-inflammatory drug (NSAID). It is used to relieve pain, tenderness, swelling and stiffness caused by osteoarthritis (arthritis caused by a breakdown of the lining of the joints) and rheumatoid arthritis. It was first sold under the brand name Dolobid, marketed by Merck & Co. The primary mode of action of Diflunisal involves blocking of the action of enzyme cyclo-oxygenase (COX) involved in the production of various chemicals in the body including prostaglandins. Prostaglandins are produced in response to injury and certain diseases and conditions, and cause pain, swelling and inflammation. By blocking the action of COX, it stops the production of these prostaglandins resulting in less pain and inflammation.

Wide spectrum therapeutic potential of this compound motivated us to enhance its bioavailability over extended period of time by functionalizing it with safe and biocompatible molecules such as glycolic acid, lactic acid, caprolactone and p-dioxanone dimers, trimers and tetramers. These molecules are the key components of commercially available absorbable medical devices. Functionalized Diflunisal oligomers are expected to release Diflunisal in a controlled manner at the site of action which will increase the efficacy of this drug over a long period of time. It will also help to increase the solubility of the drug. Finally, these hydrolysable Diflunisal compounds are expected to have improved bioavailability, improved efficacy and are also anticipated to degrade into safe and biocompatible molecules.
References:

2. Bezwada, Rao S. Controlled release of biologically active compounds from multi-armed oligomers. US Patent No. 8, 163, 806.

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19-2411 2-[5-(2,4-Difluorophenyl)-2-hydroxy-benzoyl]oxyacetic acid  
C_{15}H_{10}F_{2}O_{5}  
MW 308.23

19-2312 2-[5-(2,4-Difluorophenyl)-2-hydroxy-benzoyl]oxypropanoic acid  
C_{16}H_{12}F_{2}O_{5}  
MW 322.26

19-2413 2-[2-[5-(2,4-Difluorophenyl)-2-hydroxy-benzoyl]oxyethoxy]acetic acid  
C_{17}H_{14}F_{2}O_{6}  
MW 352.29

19-2414 6-[5-(2,4-Difluorophenyl)-2-hydroxy-benzoyl]oxyhexanoic acid  
C_{19}H_{18}F_{2}O_{5}  
MW 364.34

19-2872 2-[5-(2,4-Difluorophenyl)-2-(2-methoxyacetyl)oxy-benzoyl]oxyacetic acid  
C_{18}H_{14}F_{2}O_{7}  
MW 380.30
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19-2421 2-[2-[2-[5-(2,4-Difluorophenyl)-2-hydroxy-benzoyl]oxyethoxy]acetyl]oxyethoxy]-2-oxo-ethoxy]ethyl 5-(2,4-difluorophenyl)-2-hydroxy-benzoate
C$_{30}$H$_{30}$F$_{12}$O$_{12}$
MW 730.61

19-2422 [6-[2-[6-[5-(2,4-Difluorophenyl)-2-hydroxy-benzoyl]oxyhexanoyloxy]ethoxy]-6-oxo-hexyl] 5-(2,4-difluorophenyl)-2-hydroxy-benzoate
C$_{30}$H$_{38}$F$_{4}$O$_{10}$
MW 754.72

19-2423 [2-[2-[5-(2,4-Difluorophenyl)-2-hydroxy-benzoyl]oxyacetyl]oxyethoxy]-2-oxo-ethyl] 4-(2,4-difluorophenyl)-2-hydroxy-benzoate; (2-oxo-2-propoxy-ethyl) 4-(2,4-difluorophenyl)-2-hydroxy-benzoate
(Diflunisal Trimer)
C$_{36}$H$_{38}$F$_{4}$O$_{10}$
MW 992.82

19-2424 [2-[2-[5-(2,4-Difluorophenyl)-2-hydroxy-benzoyl]oxypropanoyloxy]ethoxy]-1-methyl-2-oxo-ethyl] 4-(2,4-difluorophenyl)-2-hydroxy-benzoate; (1-methyl-2-oxo-2-propoxy-ethyl) 4-(2,4-difluorophenyl)-2-hydroxy-benzoate
(Diflunisal Trimer)
C$_{36}$H$_{44}$F$_{6}$O$_{15}$
MW 1034.90
19-2425  
2-[2-[2-[5-(2,4-Difluorophenyl)-2-hydroxy-benzoyl]oxyethoxy]acetyl]oxyethoxy]-2-oxo-ethoxy]ethyl 4-(2,4-difluorophenyl)-2-hydroxy-benzoate; 2-(2-oxo-2-propoxy-ethoxy)ethyl 4-(2,4-difluorophenyl)-2-hydroxy-benzoate  
(Diflunisal Trimer)  
C_{56}H_{50}F_{6}O_{16}  
MW 1124.98

19-2426  
[6-2-[6-5-(2,4-Difluorophenyl)-2-hydroxy-benzoyl]oxyhexanoyloxy]ethoxy]-6-oxo-hexyl] 4-(2,4-difluorophenyl)-2-hydroxy-benzoate; (6-oxo-6-propoxy-hexyl) 4-(2,4-difluorophenyl)-2-hydroxy-benzoate  
(Diflunisal Trimer)  
C_{66}H_{62}F_{8}O_{20}  
MW 1161.14

19-2427  
(Diflunisal Tetramer)  
C_{64}H_{44}F_{8}O_{20}  
MW 1285.01
\( \text{C}_{68}\text{H}_{52}\text{F}_{8}\text{O}_{20} \)  
MW 1341.12

\( \text{C}_{72}\text{H}_{60}\text{F}_{8}\text{O}_{24} \)  
MW 1461.22

\( \text{C}_{80}\text{H}_{76}\text{F}_{8}\text{O}_{20} \)  
MW 1509.43
Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID). It has analgesic and anti-pyretic properties. It is used for relief of symptoms of arthritis, fever and pain. Ibuprofen is known to have an antiplatelet effect, though it is relatively mild and somewhat short-lived when compared with aspirin or other better-known antiplatelet drugs. In general, ibuprofen also acts as a vasoconstrictor, having been shown to constrict coronary arteries and some other blood vessels mainly because it inhibits the vasodilating prostacyclin produced by cyclooxygenase 2 enzymes.

Ibuprofen works by blocking the action of enzyme cyclo-oxygenase (COX) involved in the production of various chemicals in the body, including prostaglandins. Prostaglandins are produced in response to injury and certain diseases and conditions resulting in pain, swelling and inflammation. By blocking the action of COX, it stops the production of these prostaglandins resulting in less pain and inflammation.

Wide spectrum therapeutic potential of this compound motivated us to enhance its bioavailability over extended period of time by functionalizing it with safe and biocompatible molecules such as glycolic acid, lactic acid, caprolactone and p-dioxanone. These molecules are the key components of commercially available absorbable medical devices. Functionalized Ibuprofen oligomers are expected to release Ibuprofen in a controlled manner at the site of action which will increase the efficacy of this drug over a long period of time. It will also help to increase the solubility of the drug. Finally, these hydrolysable Ibuprofen compounds have improved bioavailability, improved efficacy and are also anticipated to degrade into safe and biocompatible molecules.
References:

2. Bezwada, Rao S. Controlled release of biologically active compounds from multi-armed oligomers. US Patent No.8, 163, 806.

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19-2431  2-[2-(4-Isobutylphenyl)propanoyloxy]acetic acid  
C_{15}H_{20}O_4  
MW 264.32

19-2432  2-[2-(4-Isobutylphenyl)propanoyloxy]propanoic acid  
C_{16}H_{22}O_4  
MW 278.34

19-2433  2-[2-[2-(4-Isobutylphenyl)propanoyloxy]ethoxy]acetic acid  
C_{17}H_{22}O_5  
MW 308.37

19-2434  6-[2-(4-Isobutylphenyl)propanoyloxy]hexanoic acid  
C_{19}H_{28}O_4  
MW 320.42

19-2435  2-[2-[2-(4-Isobutylphenyl)propanoyloxy]acetyl]oxyacetic acid  
C_{17}H_{22}O_6  
MW 322.35

19-2436  2-[2-[2-(4-Isobutylphenyl)propanoyloxy]propanoyloxy]propanoic acid  
C_{19}H_{26}O_6  
MW 350.41

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<td>19-2442</td>
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<td>666.88</td>
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\(C_{50}H_{66}O_{12}\)  
MW 861.07

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19-2444  
\[2\cdot[2\cdot[2\cdot(4\text{-isobutylphenyl})\text{propanoyloxy}]\text{propanoyloxy[ethoxy]-1-methyl-2-oxo-ethyl}]\text{ 2-(4-isobutylphenyl)propanoate; (1-methyl-2-oxo-2-propoxy-ethyl) 2-(4-isobutylphenyl)propanoate (Ibuprofen Trimer)}\]  
\(C_{53}H_{74}O_{12}\)  
MW 903.15

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19-2445  
\[2\cdot[2\cdot[2\cdot[2\cdot(4\text{-isobutylphenyl})\text{propanoyloxy[ethoxy]acetyl[oxethoxy]-2-oxo-ethoxy]ethyl 2-(4-isobutylphenyl)propanoate; 2-(2-oxo-2-propoxy-ethoxy)ethyl 2-(4-isobutylphenyl)propanoate (Ibuprofen Trimer)}\]  
\(C_{56}H_{80}O_{15}\)  
MW 993.22

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19-2446  2-[6-[2-(4-Isobutylphenyl)propanoyloxy]hexanoyloxy]ethyl 6-[2-(4-isobutylphenyl)propanoyloxy]hexanoate
(Ibuprofen Trimer)
C_{62}H_{92}O_{12}
MW 1029.39
Lumiracoxib is a member of the arylalkanoic acid class of NSAIDs. It is a COX-2 selective inhibitor drug and has structure which is different from that of other COX-2 inhibitors, such as Celecoxib. Lumiracoxib is an analogue of diclofenac and is the only acidic coxib, and has the highest COX-2 selectivity of any NSAID. It has good oral bioavailability with maximum plasma concentrations are reached two hours after oral administration. Lumiracoxib is marketed by Novartis Pharmaceuticals under the brand name of Prexige.

Wide spectrum therapeutic potential of this compound motivated us to enhance its bioavailability over extended period of time by functionalizing it with safe and biocompatible molecules such as glycolic acid, lactic acid, caprolactone and p-dioxanone. These molecules are the key components of commercially available absorbable medical devices. Functionalized Lumiracoxib oligomers are expected to release Lumiracoxib in a controlled manner at the site of action which will increase the efficacy of this drug over a long period of time. It will also help to increase the solubility of the drug. Finally, these hydrolysable Lumiracoxib compounds are expected to have improved bioavailability, improved efficacy and are also anticipated to degrade into safe and biocompatible molecules.
References:

2. Bezwada, Rao S. Controlled release of biologically active compounds from multi-armed oligomers. US Patent No.8, 163, 806.

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2-[2-[2-[2-Chloro-6-fluoro-phenyl]methyl]-5-methyl-phenyl]acetyl|oxypropanoxy|propanoic acid  
C_{22}H_{22}ClFO_{6}  
MW 436.86

19-2453  
2-[2-[2-[2-[2-Chloro-6-fluoro-phenyl]methyl]-5-methyl-phenyl]acetyl|oxyethoxy|acetyl|oxyethoxy|acetic acid  
C_{24}H_{26}ClFO_{8}  
MW 496.91

19-2454  
6-[6-[2-[2-[2-Chloro-6-fluoro-phenyl]methyl]-5-methyl-phenyl]acetyl|oxyhexanoxy|hexanoic acid  
C_{28}H_{34}ClFO_{6}  
MW 521.02

19-2455  
C_{38}H_{34}ClFO_{8}  
MW 727.57

19-2456  
2-[2-[2-[2-Chloro-6-fluoro-phenyl]methyl]-5-methyl-phenyl]acetyl|oxypropanolxy|ethyl 2-[2-[2-chloro-6-fluoro-phenyl]methyl]-5-methyl-phenyl]acetyl|oxypropanoate  
C_{40}H_{38}Cl_{2}F_{2}O_{8}  
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19-2461


(Lumiracoxib Trimer)

C_{65}H_{68}Cl_3F_3O_{15}
MW 1252.58

19-2462


(Lumiracoxib Trimer)

C_{71}H_{80}Cl_4F_4O_{12}
MW 1288.74

19-2463


(Lumiracoxib Tetramer)

C_{76}H_{68}Cl_4F_4O_{16}
MW 1455.15
19-2464

(Lumiracoxib Tetramer)

C_{80}H_{76}Cl_{4}F_{4}O_{16}
MW 1511.26

19-2465

(Lumiracoxib Tetramer)

C_{84}H_{84}Cl_{4}F_{4}O_{20}
MW 1631.36

19-2466

(Lumiracoxib Tetramer)

C_{92}H_{100}Cl_{4}F_{4}O_{16}
MW 1679.57

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Tolmetin is a non-steroidal anti-inflammatory drug of the arylalkanoic acids. It is used primarily to reduce hormones that cause pain, swelling, tenderness, and stiffness in conditions such as osteoarthritis and rheumatoid arthritis, including juvenile rheumatoid arthritis. It is marketed as brand name of Tolectin in United States.

Although the mechanism of action of Tolmetin is unknown, research involving humans and animals has shown that Tolmetin does not achieve anti-inflammatory response by stimulation of the adrenal or pituitary gland, but it has shown Tolmetin restrains prostaglandin synthetase in vitro and reduces plasma of prostaglandin E, possibly causing the anti-inflammatory response.

Wide spectrum therapeutic potential of this compound motivated us to enhance its bioavailability over extended period of time by functionalizing it with safe and biocompatible molecules such as glycolic acid, lactic acid, caprolactone and p-dioxanone. These molecules are the key components of commercially available absorbable medical devices. Functionalized Tolmetin oligomers are expected to release Tolmetin in a controlled manner at the site of action which will increase the efficacy of this drug over a long period of time. It will also help to increase the solubility of the drug. Finally, these hydrolysable Tolmetin compounds are expected to have improved bioavailability, improved efficacy and are also anticipated to degrade into safe and biocompatible molecules.
References:

2. Bezwada, Rao S. Controlled release of biologically active compounds from multi-armed oligomers. US Patent No. 8, 163, 806.

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infringement of any patent or other intellectual property right. Nothing in this publication is to be viewed as a license under any intellectual property right.
19-2467  2-[2-[5-(4-Methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxyacetic acid  
C_{16}H_{13}NO_{5}  
MW 301.29

19-2468  2-[2-[5-(4-Methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxypropanoic acid  
C_{17}H_{17}NO_{5}  
MW 315.32

19-2469  2-[2-[2-[5-(4-Methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxythoxy]acetic acid  
C_{18}H_{19}NO_{5}  
MW 345.35

19-2470  6-[2-[5-(4-Methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxyhexanoic acid  
C_{20}H_{23}NO_{5}  
MW 357.40

19-2471  2-[2-[2-[5-(4-Methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxyacetyl]oxyacetic acid  
C_{18}H_{17}NO_{7}  
MW 359.33

19-2472  2-[2-[2-[5-(4-Methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxypropanoyloxy]propanoic acid  
C_{20}H_{21}NO_{7}  
MW 387.38
19-2473
C₂₃H₂₅NO₉
MW 447.44

19-2474
6-[6-[2-[5-(4-Methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxyhexanoyloxy]hexanoic acid
C₂₆H₃₃NO₇
MW 471.54

19-2475
[2-[2-[2-[5-(4-Methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxyacetyl]oxyethoxy]-2-oxo-ethyl
2-[5-(4-methylbenzoyl)-1H-pyrrol-2-yl]acetate
C₃₄H₃₂N₂O₁₀
MW 628.62

19-2476
2-[2-[5-(4-Methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxypropanoic acid]ethyl 2-[2-[5-(4-
methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxypropanoate
C₃₆H₃₆N₂O₁₀
MW 656.68

19-2477
C₃₈H₄₀N₂O₁₂
MW 716.73
19-2478 2-[6-[2-[5-(4-Methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxyhexanoyloxy]ethyl 6-[2-[5-(4-methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxyhexanoate
\[C_{35}H_{48}N_{2}O_{10}\], MW 740.84

19-2479 [2-[2-[2-[5-(4-Methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxyacetyl]oxyethoxy]-2-oxo-ethyl 2-[5-(4-methylbenzoyl)-1H-pyrrol-2-yl]acetate; (2-oxo-2-propoxy-ethyl) 2-[5-(4-methylbenzoyl)-1H-pyrrol-2-yl]acetate
(Tolmetin Trimer)
\[C_{35}H_{53}N_{3}O_{15}\], MW 972.02

(Tolmetin Trimer)
\[C_{36}H_{59}N_{3}O_{15}\], MW 1014.11

(Tolmetin Trimer)
\[C_{36}H_{63}N_{3}O_{18}\], MW 1104.19
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<td>C_{66}H_{77}N_{15}O_{15}</td>
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<td>19-2484</td>
<td>2-[2-[2-[5-(4-Methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxypropanoyloxy]ethyl 2-[2-[5-(4-methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxypropanoate (Tolmetin Trimer)</td>
<td>C_{72}H_{72}N_{14}O_{20}</td>
<td>1313.4</td>
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<td>19-2485</td>
<td>2-[2-[2-[2-[5-(4-Methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxyethoxy]acetyl]oxyethoxy]-2-oxo-ethoxy]ethyl 2-[5-(4-methylbenzoyl)-1H-pyrrol-2-yl]acetate (Tolmetin Trimer)</td>
<td>C_{76}H_{80}N_{14}O_{24}</td>
<td>1433.5</td>
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19-2486  2-[6-[2-[5-(4-Methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxyhexanoyloxy]ethyl 6-[2-[5-(4-methylbenzoyl)-1H-pyrrol-2-yl]acetyl]oxyhexanoate
(Tolmetin Trimer)
C₈₄H₉₆N₄O₂₀
MW 1481.72
Mefenamic is used in treatment of pain, including menstrual cramps. Mefenamic acid decreases inflammation and uterine contractions by a still unknown mechanism. There is also evidence that supports the use of mefenamic acid for perimenstrual migraine headache prophylaxis. Mefenamic acid is marketed in the USA as Ponstel and is commonly known in UK as Ponstan. Other brand names include Mefalth, Mefalth T, Ponstal, Parkemed, Mafepain, Mefamed, Mephadolor, Meftal, Dyfenamic, Potarlon, Dolfenal, Meyerdonal, Alfoxan, Fenagesic, Spiralgin.

Mefenamic acid works by blocking the action of cyclo-oxygenase enzyme. Cyclo-oxygenase (COX) is involved in the production of various chemicals in the body, including prostaglandins. Prostaglandins are produced in response to injury and certain diseases and conditions, and cause pain, swelling and inflammation. By blocking the action of COX, it stops the production of these prostaglandins resulting in less pain and inflammation.

Wide spectrum therapeutic potential of this compound motivated us to enhance its bioavailability over extended period of time by functionalizing it with safe and biocompatible molecules such as glycolic acid, lactic acid, caprolactone and p-dioxanone. These molecules are the key components of commercially available absorbable medical devices. Functionalized Mefenamic acid oligomers are expected to release Mefenamic acid in a controlled manner at the site of action which will increase the efficacy of this drug over a long period of time. It will also help to increase the solubility of the drug. Finally, these hydrolysable Mefenamic acid compounds are expected to have improved bioavailability, improved efficacy and are also anticipated to degrade into safe and biocompatible molecules.
References:

2. Bezwada, Rao S. Controlled release of biologically active compounds from multi-armed oligomers. US Patent No. 8,163,806.

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<td>19-2487</td>
<td>[2-[2-[2-[2,3-Dimethylphenyl]methyl]benzoyl]oxyacetyl]oxyethoxy]-2-oxo-ethyl 2-[(2,3-dimethylphenyl)methyl]benzoate</td>
<td>C_{38}H_{38}O_8, MW 622.72</td>
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<td>19-2488</td>
<td>[2-[2-[2-[2,3-Dimethylphenyl]methyl]benzoyl]oxypropanoyloxy]ethoxy]-1-methyl-2-oxo-ethyl 2-[(2,3-dimethylphenyl)methyl]benzoate</td>
<td>C_{40}H_{42}O_8, MW 650.78</td>
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<td>2-[2-[2-[2-[2,3-Dimethylphenyl]methyl]benzoyl]oxyethoxy]acetyl]oxyethoxy]-2-oxo-ethoxy]ethyl 2-[(2,3-dimethylphenyl)methyl]benzoate</td>
<td>C_{42}H_{46}O_10, MW 710.83</td>
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<td>19-2490</td>
<td>[6-[6-[2-[2,3-Dimethylphenyl]methyl]benzoyl]oxyhexanoyloxy]ethoxy]-6-oxo-hexyl 2-[(2,3-dimethylphenyl)methyl]benzoate</td>
<td>C_{46}H_{54}O_8, MW 734.94</td>
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<tr>
<td>19-2491</td>
<td>2-[2-[2,3-Dimethylphenyl]methyl]benzoyl]oxyacetic acid</td>
<td>C_{18}H_{18}O_4, MW 298.33</td>
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<td>$C_{19}H_{20}O_4$</td>
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<td><img src="image2.png" alt="Structure Image" /></td>
<td>$C_{20}H_{22}O_5$</td>
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<td><img src="image3.png" alt="Structure Image" /></td>
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<td>$C_{21}H_{22}O_6$</td>
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<td><img src="image6.png" alt="Structure Image" /></td>
<td>$C_{22}H_{24}O_6$</td>
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19-2498  6-[6-{2-[(2,3-Dimethylphenyl)methyl]benzoyl}oxyhexanoyloxy]hexanoic acid
C_{28}H_{36}O_{6}
MW 468.58
Loxoprofen

Loxoprofen belongs to propionic acid derivatives group. Loxoprofen is in the same chemical family as ibuprofen, naproxen and ketoprofen. It is used in musculoskeletal and joint disorders. Loxoprofen is a prodrug. It is administered in an inactive form. Once administered, the prodrug is metabolized in vivo into an active metabolite.

It is marketed under various trade names as its sodium salt, loxoprofen sodium, under the trade name Loxonin, as Oxeno and as Loxomac. Loxoprofen is a non-selective cyclooxygenase inhibitor, and works by reducing the synthesis of prostaglandins hence reducing pain and inflammation.

Wide spectrum therapeutic potential of this compound motivated us to enhance its bioavailability over extended period of time by functionalizing it with safe and biocompatible molecules such as glycolic acid, lactic acid, caprolactone and p-dioxanone. These molecules are the key components of commercially available absorbable medical devices. Functionalized Loxoprofen oligomers are expected to release Loxoprofen in a controlled manner at the site of action which will increase the efficacy of this drug over a long period of time. It will also help to increase the solubility of the drug. Finally, these hydrolysable Loxoprofen compounds have improved bioavailability, improved efficacy and are also anticipated to degrade into safe and biocompatible molecules.
References:

2. Bezwada, Rao S. Controlled release of biologically active compounds from multi-armed oligomers. US Patent No.8, 163, 806.

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84
19-2499 2-[2-[4-[(2-Oxocyclopentyl)methyl]phenyl]propanoyloxy]acetic acid

\[ \text{C}_{17}\text{H}_{20}\text{O}_5 \]
MW 304.34

19-2500 2-[2-[4-[(2-Oxocyclopentyl)methyl]phenyl]propanoyloxy]propanoic acid

\[ \text{C}_{18}\text{H}_{22}\text{O}_5 \]
MW 318.36


\[ \text{C}_{19}\text{H}_{24}\text{O}_6 \]
MW 348.39

19-2502 6-[2-[4-[(2-Oxocyclopentyl)methyl]phenyl]propanoyloxy]hexanoic acid

\[ \text{C}_{21}\text{H}_{28}\text{O}_5 \]
MW 360.44


\[ \text{C}_{20}\text{H}_{22}\text{O}_7 \]
MW 362.37


\[ \text{C}_{21}\text{H}_{26}\text{O}_7 \]
MW 390.43
C_{23}H_{30}O_9
MW 450.48

C_{27}H_{38}O_7
MW 474.59
Tiaprofenic Acid

Tiaprofenic acid is a non-steroidal anti-inflammatory drug. It belongs to arylpropionic acid (profen) class. It is used to treat pain, especially arthritic pain, with indications for osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, periarticular disorders, and strains and sprains. It is marketed under the trade names Surgam, Surgamyl and Tiaprofen, and in generic formulations.

Tiaprofenic acid works by blocking the action of cyclo-oxygenase enzyme. Cyclo-oxygenase (COX) is involved in the production of various chemicals in the body, including prostaglandins. Prostaglandins are produced in response to injury and certain diseases and conditions, and cause pain, swelling and inflammation. By blocking the action of COX, it stops the production of these prostaglandins resulting in less pain and inflammation.

Wide spectrum therapeutic potential of this compound motivated us to enhance its bioavailability over extended period of time by functionalizing it with safe and biocompatible molecules such as glycolic acid, lactic acid, caprolactone and p-dioxanone. These molecules are the key components of commercially available absorbable medical devices. Functionalized Tiaprofenic acid oligomers are expected to release Tiaprofenic acid in a controlled manner at the site of action which will increase the efficacy of this drug over a long period of time. It will also help to increase the solubility of the drug. Finally, these hydrolysable Tiaprofenic acid compounds are expected to have improved bioavailability, improved efficacy and are also anticipated to degrade into safe and biocompatible molecules.
References:

2. Bezwada, Rao S. Controlled release of biologically active compounds from multi-armed oligomers. US Patent No.8, 163, 806.

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88
19-2507 2-[2-(5-Benzoyl-2-thienyl)propanoyloxy]ethanethioic O-acid
C_{16}H_{14}O_{4}S_{2}
MW 334.41

19-2508 2-[2-(5-Benzoyl-2-thienyl)propanoyloxy]propanethioic O-acid
C_{17}H_{16}O_{4}S_{2}
MW 348.44

19-2509 2-[2-[2-(5-Benzoyl-2-thienyl)propanoyloxy]ethoxy]acetic acid
C_{18}H_{16}O_{6}S
MW 362.40

19-2510 6-[2-(5-Benzoyl-2-thienyl)propanoyloxy]hexanoic acid
C_{20}H_{22}O_{5}S
MW 374.45

19-2511 2-[2-[2-(5-Benzoyl-2-thienyl)propanoyloxy]ethanethiolyloxycetic acid
C_{19}H_{18}O_{6}S_{2}
MW 392.45

19-2512 2-[2-[2-(5-Benzoyl-2-thienyl)propanoyloxy]propanethiolyloxypanoic acid
C_{20}H_{20}O_{6}S_{2}
MW 420.50
C_{22}H_{24}O_{9}S
MW 464.48

19-2514  6-[6-[2-(5-Benzoyl-2-thienyl)propanoyloxy]hexanoyloxy]hexanoic acid
C_{26}H_{32}O_{7}S
MW 488.59

C_{34}H_{30}O_{10}S_{2}
MW 662.74

C_{36}H_{34}O_{10}S_{2}
MW 690.79

C_{38}H_{38}O_{12}S_{2}
MW 750.85

C_{42}H_{46}O_{10}S_{2}
MW 774.96
Ketorolac

Ketorolac is a non-steroidal anti-inflammatory drug (NSAID) in the family of heterocyclic acetic acid derivatives, often used as an analgesic. Ketorolac acts by inhibiting the synthesis of prostaglandins in the body. Ketorolac in its oral (tablet or capsule) and intramuscular (injected) preparations is a racemic mixture of both (S)-(−)-ketorolac, the active isomer, and (R)-(++)-ketorolac. Ketorolac is indicated for short-term management of moderate to severe pain.

The primary mechanism of action responsible for Ketorolac's anti-inflammatory, antipyretic and analgesic effects is the inhibition of prostaglandin synthesis by competitive blocking of the enzyme cyclooxygenase (COX). Ketorolac is a non selective COX inhibitor.

Wide spectrum therapeutic potential of this compound motivated us to enhance its bioavailability over extended period of time by functionalizing it with safe and biocompatible molecules such as glycolic acid, lactic acid, caprolactone and p-dioxanone. These molecules are the key components of commercially available absorbable medical devices. Functionalized Ketorolac oligomers are expected to release Ketorolac in a controlled manner at the site of action which will increase the efficacy of this drug over a long period of time. It will also help to increase the solubility of the drug. Finally, these hydrolysable Ketorolac compounds are expected to have improved bioavailability, improved efficacy and are also anticipated to degrade into safe and biocompatible molecules.
References:

2. Bezwada, Rao S. Controlled release of biologically active compounds from multi-armed oligomers. US Patent No.8, 163, 806.

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<td><img src="image1" alt="2-(5-Benzoyl-2,3-dihydro-1H-pyrrolizine-1-carbonyl)oxyacetic acid" /></td>
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<td><img src="image2" alt="2-(5-Benzoyl-2,3-dihydro-1H-pyrrolizine-1-carbonyl)oxypropanoic acid" /></td>
<td>C_{18}H_{17}NO_{5}</td>
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<td>C_{19}H_{19}NO_{6}</td>
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<td><img src="image4" alt="6-(5-Benzoyl-2,3-dihydro-1H-pyrrolizine-1-carbonyl)oxyhexanoic acid" /></td>
<td>C_{21}H_{23}NO_{5}</td>
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<td>C_{19}H_{17}NO_{7}</td>
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<td>C_{23}H_{21}NO_{7}</td>
<td>399.39</td>
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19-2514  2-[2-[2-[5-Benzoyl-2,3-dihydro-1H-pyrrolizine carbonyl]oxyethoxy]acetyl]oxyethoxy]acetic acid  
\[C_{23}H_{25}NO_9\]  
MW 459.44

19-2515  6-[6-[5-Benzoyl-2,3-dihydro-1H-pyrrolizine-1-carbonyl]oxyhexanoyloxy]hexanoic acid  
\[C_{27}H_{33}NO_7\]  
MW 483.55

\[C_{30}H_{32}N_2O_{10}\]  
MW 652.66

\[C_{36}H_{32}N_2O_{10}\]  
MW 680.72

\[C_{40}H_{40}N_2O_{12}\]  
MW 740.77
19-2519

[6-[2-[6-(5-Benzoyl-2,3-dihydro-1H-pyrrolizine-1-carbonyl)oxyhexanoyloxy]ethoxy]-6-oxo-hexyl] 5-benzoyl-2,3-dihydro-1H-pyrrolizine-1-carboxylate

C_{44}H_{48}N_2O_{10}

MW 764.88

![Molecular Structure](image)