

PHARMACOLOGY OF METHADONE

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METHADONE



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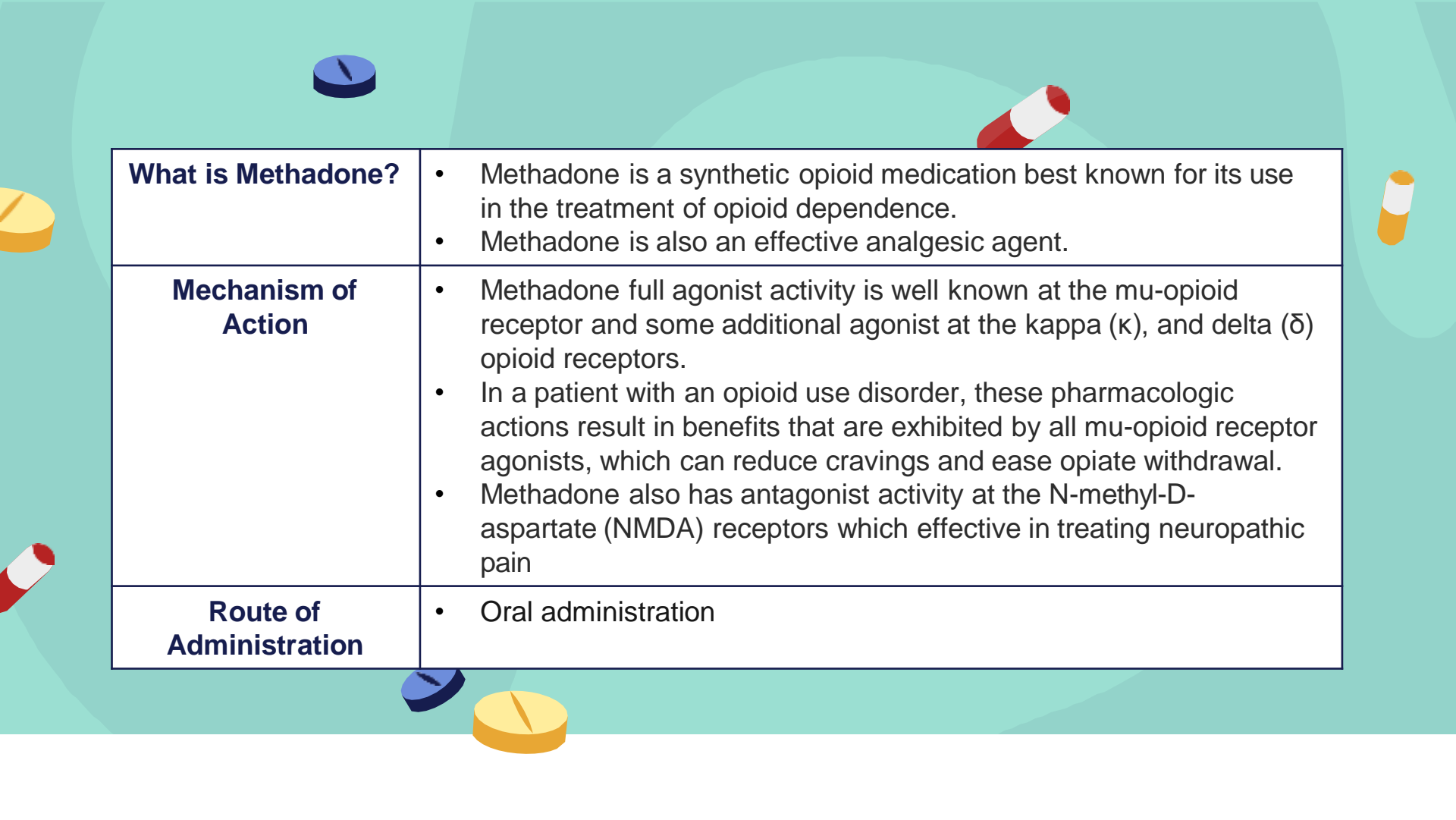
Methadone

- 1st produced by German Chemists in early 20th century and has been used clinically since end of WW1.
- Synthetic opiate without strong sedative effects.
- White crystalline powder.
- Widely used as a **substitution therapy** in the treatment of heroin addiction.



Pharmacology of Methadone





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| What is Methadone? | <ul style="list-style-type: none">• Methadone is a synthetic opioid medication best known for its use in the treatment of opioid dependence.• Methadone is also an effective analgesic agent. |
| Mechanism of Action | <ul style="list-style-type: none">• Methadone full agonist activity is well known at the mu-opioid receptor and some additional agonist at the kappa (κ), and delta (δ) opioid receptors.• In a patient with an opioid use disorder, these pharmacologic actions result in benefits that are exhibited by all mu-opioid receptor agonists, which can reduce cravings and ease opiate withdrawal.• Methadone also has antagonist activity at the N-methyl-D-aspartate (NMDA) receptors which effective in treating neuropathic pain |
| Route of Administration | <ul style="list-style-type: none">• Oral administration |



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| Absorption | <ul style="list-style-type: none">• Methadone is a fat-soluble medication that is quickly absorbed when taken orally.• But the range of the time to peak concentration is from one to five hours.• Longer duration to peak concentration in chronic users of methadone may be caused by slowed stomach emptying caused by the drug.• In general, the analgesic action of a dose lasts for four to six hours and starts working after 30 to 60 minutes of administer. |
| Distribution | <ul style="list-style-type: none">• Methadone is also widely distributed to tissue, and, with continuous use, tissue levels may exceed levels in plasma.• This extensive protein and tissue binding is responsible for the long plasma half life of the drug, particularly with continuous use. |



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| Metabolism | <ul style="list-style-type: none">• Metabolism of methadone to inactive forms is the principle means of elimination.• The drug is metabolized both by the liver and by intestinal CYP 3A4 and, to a lesser extent, by CYP 2D6.• Some of the variability of enzyme activity in different people likely accounts for the large differences in clearance and half life of methadone seen within a population |
| Excretion | <ul style="list-style-type: none">• Methadone undergoes urinary and fecal excretion.• The major metabolite of methadone is EDDP (2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine) which can be detected in the urine of patients who are metabolizing methadone. |
| Half life | <ul style="list-style-type: none">• 8 – 59 hours. |

Drug/Substance Interaction with Methadone



| <i>Bahan/Dadah</i> | <i>Kesan ke atas Methadone</i> | <i>Cara mengatasi</i> |
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| <i>Alkohol</i> | <i>Meningkat</i> | <i>Elakkan</i> |
| <i>Antiepileptik,cth : Phenytoin</i> | <i>Menurun</i> | <i>Tingkatkan dos Methadone atau bahagikan dos</i> |
| <i>Benzodiazepine</i> | <i>Meningkat</i> | <i>Hadkan penggunaan benzodiazepine</i> |
| <i>Cimetidine</i> | <i>Meningkat</i> | <i>Elakkan</i> |
| <i>Ciprofloxacin</i> | <i>Meningkat</i> | <i>Mungkin perlu kurangkan dos Methadone</i> |
| <i>Efavirenz</i> | <i>Menurun</i> | <i>Mungkin perlu tingkatkan dos Methadone ataupun bahagikan dos.</i> |
| <i>Fluoxetine</i> | <i>Meningkat</i> | <i>Tukar kepada SSRI lain</i> |

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| <i>Fluvoxamine</i> | <i>Meningkat</i> | <i>Tukar kepada SSRI lain</i> |
| <i>Nicotine</i> | <i>Menurun</i> | <i>Nasihatkan pesakit supaya berhenti merokok</i> |
| <i>Rifampicin</i> | <i>Menurun</i> | <i>Tingkatkan dos Methadone atau bahagikan dos</i> |
| <i>Tricyclic Antidepressants</i> | <i>Meningkat</i> | <i>Elakkan</i> |
| <i>Urine acidifiers cth. acid ascorbic</i> | <i>Menurun</i> | <i>Elakkan</i> |
| <i>Urine alkalinisers cth. Sodium bicarbonate</i> | <i>Meningkat</i> | <i>Elakkan</i> |
| <i>Zidovudine</i> | <i>Tiada (mungkin meningkatkan paras zidovudine)</i> | <i>Kurangkan dos Zidovudine</i> |

**THANK
YOU!**

