Claims

1. Water-insoluble, matrix tablets capable of releasing one or more active ingredients into the body over an extended time period containing :

- one active ingredient which may be the subject of drug abuse dispersed within a compression matrix, characterized in that said compression matrix represents 50 to 98 weight % of the total weight of said tablet and contains ~~at least one excipient chosen from the group comprising sustained release, water insoluble, pH independent, polymers, mineral excipients and their mixtures~~ a mixture of microcrystalline cellulose with [polyvinyl acetate/polyvinylpyrrolidone (80:20)] to the proportion of (1:1),
- one or more of the following substances (a) to (f) or a mixture thereof:

(a) a substance which irritates the nasal and/or pharyngeal tracts,

(b) a viscosity-increasing agent, leading to formation of a gel when the tablet is dissolved in a minimum amount of water,

(c) an emetic substance,

(d) an aversive colouring agent,

(e) a bittering-substance,

(f) an antagonist of the active ingredient(s) which may be the subject of drug abuse,

wherein said active ingredient which may be the subject of drug abuse belong to the group of analgesics.

2. Matrix tablets according to claim 1, characterized in that said compression matrix represents 85 to 95 % weight % of the total weight of said tablet.

~~3. Matrix tablets according to any of claims 1 and 2, characterized in that said compression matrix comprises a mixture of at least two excipients chosen from among microcrystalline cellulose, polymers of the family of water-insoluble, pH-independent methacrylic acids, derivatives of polyvinylalcohols, polymers of lactic and glycolic acids, starches, waxes, derivatives of polyvinylacetates,, derivatives of polyvinylpyrrolidone, mineral excipients and their mixtures.~~

~~4. Matrix tablets according to any of claims 1 to 3, characterized in that the mineral excipients are chosen from the group comprising calcium phosphates, aluminium and silicon silicates, magnesium carbonate and their mixtures.~~

~~5.~~3. Matrix tablets according to ~~any of claims 1 to 4~~claims 1 or 2, containing 0,1 to 10% by weight of the total weight of the compression matrix of at least one pharmaceutically acceptable excipient chosen from the group comprising anti-adherent agents, agents capable of improving tablet cohesion on compressing, fillers, lubricants, plasticizers, bulking agents, sweeteners and colouring agents,

~~6. Matrix tablets according to any of claims 1 to 5, characterized in that said active ingredient(s) are chosen from the group comprising psychotropics, neuroleptics, tranquillizers, hypnotics, analgesics and anxiolytics.~~

~~7.~~4. Matrix tablets according to any of claims 1 to ~~6~~3, characterized in that said active ingredients belong to the group comprising morphine, oxycodone, hydrocodone, hydromorphone, oxymorphone, tramadol, methadone, codeine, fentanyl and buprenorphine, their salts and their pharmaceutically acceptable derivatives.

~~8.~~5. Matrix tablets according to any of claims 1 to ~~7~~4, characterized in that the antagonist agent of the said active ingredient(s) which may be the subject of drug abuse is naloxone or naltrexone or one of their pharmaceutically acceptable salts.

~~9.~~6. Matrix tablets according to any of claims 1 to ~~8~~5, characterized in that they have an outer coating.

~~10.~~7. Matrix tablets according to claim ~~9~~6, characterized in that said outer coating consists of at least one sustained-release polymer advantageously chosen from the group comprising ethylcellulose derivatives and methacrylic polymers.

~~11. Matrix tablets according to any of claims 1 to 10, characterized in that said compression matrix contains a mixture of microcrystalline cellulose with [polyvinyl acetate/polyvinylpyrrolidone (80:20)] to the proportion of (1:1) and that said active ingredient which may be the subject of drug abuse belong to the group of analgesics.~~

~~12.~~8. Matrix tablets according to claim ~~11~~1, characterized in that they have an outer coating consisting of ethylcellulose.

~~13.~~9. Matrix tablets according to any of claims 1 to ~~12~~8, characterized in that they are capable of releasing the active ingredient which may be the subject of drug abuse over a period of more than 12 hours.

~~14.~~10. Matrix tablets according to any of claims 1 to ~~13~~9, characterized in that they are capable of releasing the active ingredient which may be the subject of drug abuse over a period of more than 20 hours.

~~15.~~11. Matrix tablets containing oxycodone according to claim 1~~1~~, characterized in that they have a plasma profile after once-a-day administration in man, such that the ratio of the Cmax observed after administration of said tablets to the Cmax value observed after administration of OxyContin® extended release tablets containing the same dose, does not exceed 0.7.

~~16.~~12. Matrix tablets containing oxycodone according to claim 1~~1~~, characterized in that their plasma profile after once-a-day administration in man is such that the ratio of AUC∞ observed for said tablets to the AUC∞ value observed with OxyContin® extended release tablets with the same dose, lies in the interval of 80 to 125 %.

~~17.~~13. Matrix tablets according to any of claims 1 to ~~16~~12, characterized in that they can be administered once a day.

~~18.~~14. Method to produce matrix tablets according to any of claims 1 to ~~17~~13, characterized in that it comprises the following steps:

- mixing the active ingredient(s) with the excipient(s) of the compression matrix,
- optional granulation, and
- compressing said mixture under conditions chosen so that said tablet has a crush resistance of at least 4 MPa, advantageously at least 6 MPa.

~~19.~~15. Method according to claim ~~18~~14, characterized in that the compression step is conducted without the compression mixture or the compression tooling being subjected to a heating step either before or during the actual compression step.

~~20.~~16. Method according to either of claims ~~18~~-14 and ~~19~~15, characterized in that it also comprises a coating step of said matrix tablet.

~~21.~~17. Method according to claim ~~20~~16, characterized in that it also comprises a curing step of said outer coating.

~~22.~~18. Use of a pharmaceutical composition in the form of tablets according to any of claims 1 to ~~17~~13, for the sustained administering of active ingredients which may be the subject of the drug abuse, intended to prevent the accidental misuse and/or to deter drug abuse of these active ingredients.