QSPainRelief

Effective combinational treatment of chronic pain in individual patients, by an innovative quantitative systems pharmacology pain relief approach.
H2020 – 848068

D3.5: Dissemination ready database

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Contents

1. Executive summary

The QSPainRelief consortium aims to develop effective combinational treatment of chronic pain in individual patients by an innovative quantitative systems pharmacology (QSP) pain relief approach. To this end multiple types of data are generated or retrieved from the public domain by the consortium partners, ranging from *in vitro* and in vivo experimental data to clinical trials in chronic pain patients and *in silico* predictions. The strength of the QSPainRelief platform lies in its integration of data through a computational modelling platform. To facilitate the integration of all the QSPainRelief data, the consortium has developed the QSPainRelief database, which serves as a repository for all data, organized according to FAIR principles. The QSPainRelief database serves as the central repository where all data generated by the consortium is stored. The QSPainRelief database is used to share data amongst QSPainRelief partners, both during as well as after the end of the project. The QSPainRelief database is also used as a platform to share data to external parties that would like to use data available in the database.

The current deliverable report D3.5 describes the delivery of the dissemination-ready QSPainRelief database. The QSPainRelief database has been implemented in such a way that it can also be used to disseminate (parts of) the available data to external researchers. In some cases, data is not made publicly available, either because of GDPR concerns or because the data is used as part of the QSPainRelief platform used for commercialization steps as defined in the sustainability plan. Overall, the aim of the QSPainRelief database is to freely share as much data as possible, which is ultimately the case for 14 out of 20 datasets in the database. In this deliverable report, we describe the dissemination-ready database, more specifically: 1) the final datasets that are present in the QSPainRelief database, 2) the open-access availability of the data in the database and 3) how data sharing is implemented.

2. Overview of available data

Within the dissemination-ready QSPainRelief database, a total of 20 different experimental, clinical and literature-derived datasets are available, summing to 2,176,125 rows of data. These datasets were contributed by the different QSPainRelief partners. For a detailed description of the structuring of the database and data types we refer to deliverable 3.4. An overview of the current datasets available is provided in Table 3.

2.1. Clinical trials data

The largest sub-database is the '*Clinical Trials*' database, consisting of 1.3 million rows of data, comprised of 5 individual datasets based on data from 477 participants, delivered by the QSPainRelief partners CHDR (WP7) and UCL (WP8). These clinical trial datasets contain detailed information on pharmacokinetics, pharmacodynamics and patient-wellbeing. The pharmacodynamic measurements consist of a wide range of different endpoints, which measure both drug effects and side-effects.

2.2. Experimental data

Different types of experimental data are available in the '*Experimental Studies*' sub-database, delivered by the QSPainRelief partners UNIBO (WP5), UPF (WP6), and ULEI (total of 33,173 rows, WP3). These data comprise *in vitro* cellular assays in different models that show the impact of morphine and cotreatments on the expression and activity of multiple receptors (UNIBO). In addition, the database contains *in vivo* results of studies done in mice, assessing the effect of morphine in both healthy and neuropathic mice (UPF). Pharmacokinetic information of morphine and its metabolite M3G in both plasma and brain of these mice is also available (ULEI).

2.3. Drug and systems parameters

The 'Drug and System Parameters' sub-database contains a wide range of data derived from literature (2,645 rows), with respect to drug physicochemical properties, drug pharmacokinetics in both plasma and CNS, CNS physiological parameters and binding kinetic information.

2.4. Model predictions

The '*Model Predictions*' sub-database contains output from *in silico* models (total of 824,116 rows), delivered by QSPainRelief partners ISB and ULEI. It contains information on pharmacokinetic predictions, made using the LeiCNS-PK3.0 PBPK model, on multiple drugs after single and multiple dosing regimens, as well as corresponding receptor occupancy in different parts of the CNS. This data was in turn used as input for the predictions by ISB on morphine and combinational treatment analgesia and side effects.

2.5. Data availability at project finalization

At the moment of finalization of the QSPainRelief project, 30 June 2025, not all data is ready to be publicly disseminated. The last column in table 3.1 details to what extent the individual datasets can be made publicly available at the end of the project. We have categorized public availability as follows:

1. Yes, directly
2. Yes, after embargo period of 1-year post-project end, due to publicly available open access only after publication of the data by the partner
3. Yes, but only summarize level data (due to GDPR concerns)
4. No possibility for open access

The five datasets within the 'Drug and Systems Parameters' sub-database are all based on data derived from literature, and can as such immediately be shared without restrictions. Of the 20 datasets, 6 have been indicated by partners to never be available for open access. Of these 6, 2 would only be available on a summary level. These are the Clinical Trial datasets by QSPainRelief partner UCL, as the ethics committee for these studies requested that only aggregated data can be shared. The remaining 4 datasets are model predictions, which are the core of the QSPainRelief consortium, and are as not shared as they are considered foreground IP which will be used to further implement the long-term sustainability (exploitation) strategy.

Table 1: Overview of all data present within the QSPainRelief database

Sub-database	DataID	Primary data type	Number of rows in data table	Description	Number of drugs/treatments	Number of species/systems	QSPainRelief partner	Publicly available
Experimental Studies	unibo.cAMP	*in vitro* experiment	829	Experimental data showing the change in cAMP after dosing with morphine, thc, pregabalin and combinations of these drugs. Measured in multiple *in vitro* cell lines	4	3 (SH-SY5Y [human neuroblastoma cells], morphine-treated SH-SY5Y, rat cortex neurons)	UNIBO	After publication
Experimental Studies	unibo.mRNA	*in vitro* experiment	2872	Experimental data on change in μ-opioid recpetor mRNA expression in different cell lines after treatment with different morphine concentrations	1	6 (mouse striatum, mouse cortex, rat striatum, rat cortex, rat DRG, SH-SY5Y)	UNIBO	After publication
Experimental Studies	unibo.confocal	Microscopy data	41	Data on μ-opioid receptor and CB1 receptor colocalization, based on different mutations of the respective receptor and different morphine doses	1	11 (all in HEK293 cells, with different combinations of μ-opioid receptor and CB1 mutations)	UNIBO	After publication
Experimental Studies	upf.dose selection_ba	Mouse experiments	10752	Data on effect of morphine in three different doses on mouse behaviour in healthy and neuropathic pain mice	1	1 (mouse)	UPF	After publication
Experimental studies	upf.selfadmin_ba	Mouse experiments	18479	Data on effect of morphine and pregabalin in a single dose on mouse behaviour in healthy and neuropathic pain mice	2	1 (mouse)	UPF	After publication
Experimental Studies	upf.morPK_ba	Mouse experiments	200	Pharmacokinetic measurements of morphine and M3G in plasma and brain in healthy and neuropathic pain mice	1	1 (mouse)	UPF	After publication

Sub-database	DataID	Primary data type	Number of rows in data table	Description	Number of drugs/treatments	Number of species/systems	QSPainRelief partner	Publicly available
Model predictions	ISB.combtreatment	*In silico* model output	1545	Output of the effect of morphine + combinational treatment as predicted by the QSP model developed by QSPainRelief partner ISB	37 combinations of morphine + codrug	1 (human)	ISB	No
Model predictions	ISB.side-effect	*In silico* model output	4120	Output of the predicted side effects caused by the simulated combinational treatments	37 combinations of morphine + codrug	1 (human)	ISB	No
Model predictions	ulei.PKRO.singledose	*In silico* model output	16740	Output of the LeiCNS-PK3.0 model on PK and receptor occupancy of multiple drugs (single dose) in plasma, brainECF and CSF compartments in humans	12	1 (human)	ULEI	No
Model predictions	ulei.PKRO.multipledose	*In silico* model output	801711	Output of the LeiCNS-PK3.0 model on PK and receptor occupancy of multiple drugs (repeated dosing) in plasma, brainECF and CSF compartments in humans	11	1 (human)	ULEI	No
Drug and System Parameters - binding kinetics	ulei.bindingkinetics_db	Literature-derived data	346	Literature-derived information on drug binding kinetic parameters	66	10 (human, sheep, chicken, rat, monkey, mouse, cow, guinea pig, rhesus monkey, zaire ebola virus)	ULEI	Yes
Drug and System Parameters - drug	ulei.systemparameters_bg	Literature-derived data	550	Literature-derived information on drug physicochemical properties	112	n/a	ULEI	Yes

Sub-database	DataID	Primary data type	Number of rows in data table	Description	Number of drugs/treatments	Number of species/systems	QSPainRelief partner	Publicly available
specific properties								
Drug and System Parameters - plasma pharmacokinetics	ulei.systemparameters_bg	Literature-derived data	130	Literature-derived information on plasma pharmacokinetic parameters	9	2 (rat, human)	ULEI	Yes
Drug and System parameters - CNS pharmacokinetics	ulei.systemparameters_bg	Literature-derived data	986	Literature-derived information on CNS pharmacokinetic parameters	102	3 (rat, mouse, human)	ULEI	Yes
Drug and System parameters - System-specific properties	ulei.systemparameters_bg and ulei.systemparameters_db	Literature-derived data	633	Literature-derived information on system-specific properties	0	4 (rat, mouse, human, rabbit)	ULEI	Yes
Clinical Studies	chdr.historicaldata	Clinical trial data	408479	Data on PK and PD of multiple drugs (also including combinational treatments)	14	1 (healthy volunteers, n = 37)	CHDR	Unknown - asked partner
Clinical Studies	chdr.morphinestudy_wb	Clinical trial data	254397	Clinical trial on morphine and pregabalin combinational treatment in healthy volunteers Contains both PK and PD measurements.	2	1 (healthy volunteers, n = 28)	CHDR	Yes, published data

Sub-database	DataID	Primary data type	Number of rows in data table	Description	Number of drugs/treatments	Number of species/systems	QSPainRelief partner	Publicly available
Clinical Studies	chdr.novelb	Clinical trial data	224837	Clinical trial on morphine and fluvoxamine combinational treatment in healthy volunteers.	2	1 (healthy volunteers, n = 24)	CHDR	After publication
Clinical Studies	UCL_BIOPAIN	Clinical trial data	80616	Clinical trial data on effect of pregabalin, lacosamide and tapentadol in healthy volunteers. Contains both PK and PD measurements.	4	1 (healthy volunteers, n = 20)	UCL	No – summary data available upon request
Clinical Studies	UCL_POPQUEST	Clinical trial data	347862	Questionnaire data on how postoperative pain is perceived and managed. No drug treatment information.	0	1 (chronic pain patients, n = 368)	UCL	No – summary data available upon request

3. Access procedures

External researchers who wish to utilize the publicly available QSPainRelief database can through the web platform register for access. When registering, the individual will be asked to briefly motivated the intended use of the data. We consider this important because the database contains clinical data, that, while pseudonymized, in the opinion of the consortium should be carefully handled. In addition, when registering, the user will need to accept the terms of use of the data, e.g. a CC BY-NC-ND license (no commercial use, no derivatives). After review of the request an user account will be created and shared with the requesting individual together with a short instruction on how to work with the database. Current QSPainRelief partners will maintain continued access to the database after the end of the project.